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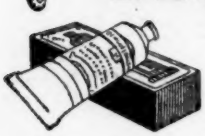

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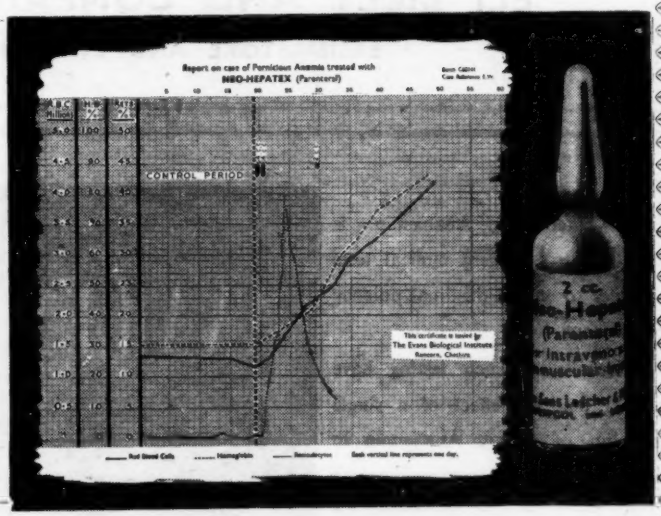

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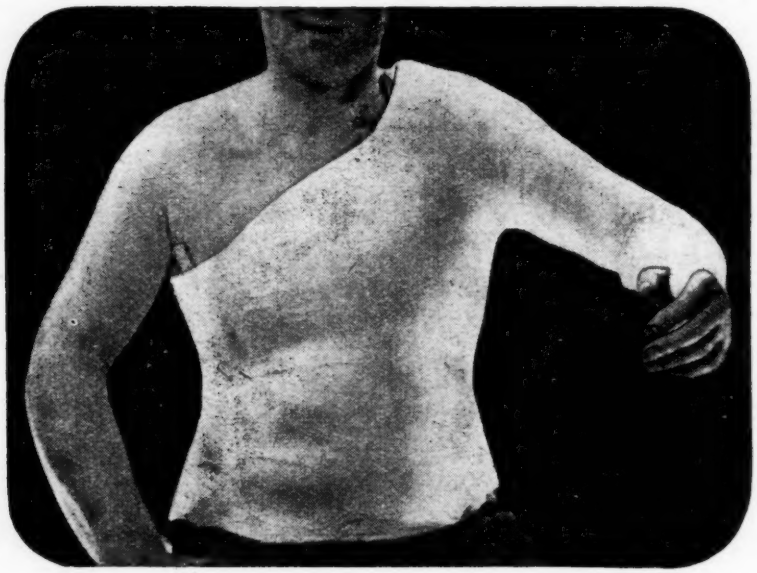

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PNEUMONIA TREATED WITH SULPHAPYRIDINE AND SULPHATHIAZOLE

CONCENTRATION OF THE DRUGS IN THE BLOOD

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THE present work was begun in the spring of 1940, when little was known of the pharmacology of sulphathiazole. We thought it would be useful to compare sulphathiazole with sulphapyridine in the treatment of lobar pneumonia; it seemed at the time that sulphathiazole might be less toxic than sulphapyridine and little if at all inferior in bactericidal action against the pneumococcus. Since the bactericidal effect depends on the concentration of the drug in the blood and tissue fluids, it was necessary to base the comparison between the two drugs on blood analyses rather than on dosage alone. The plan of work was therefore to carry out clinical trials with both sulphathiazole and sulphapyridine, with analyses of the blood at short intervals during the whole course of treatment.

Pneumonia was not very prevalent during 1940 and the number of cases studied is small—too small for an assessment of the relative therapeutic value of the two drugs. Since our work began, however, several American workers have published the results of clinical trials on very large numbers of cases, which show that sulphathiazole has no special advantage over sulphapyridine, except that it is less likely to cause nausea and vomiting. We therefore present our findings, primarily to show the concentrations of the drugs in the blood on a given dosage.

MATERIAL AND METHODS

Only the free drugs in the blood were estimated. The technique was essentially that of Marshall and Litchfield (1938) with some differences in detail.

Whole blood, 1 c.cm., is measured into 15 c.cm. of distilled water. After thorough laking of the corpuscles, 4 c.cm. of 15% trichloracetic acid is added; the mixture is shaken, allowed to stand for ten minutes and filtered. To 10 c.cm. of filtrate 1 c.cm. of sodium nitrite solution (0·1% freshly made) is added; the mixture is shaken and allowed to stand for three minutes; then 0·1 c.cm. of urea (5%) is added, the mixture is shaken and allowed to stand for two minutes; finally 1·9 c.cm. of phosphate buffer (M/1 KH_2PO_4) and 5 c.cm. of dimethyl-α-naphthylamine (0·4% by volume in 95% alcohol) are added; five to ten minutes are allowed for full development of the red colour, which is either measured in the photometer or compared in the colorimeter with a standard solution of the drug treated in the same way as the blood filtrate. Most of the measurements in this work were made in the Pulfrich photometer, using the filter S 53, and working with a control mixture in the compensating cell, prepared from the reagents alone with water in place of blood filtrate.

It was found that the method described by Marshall (1937) for the estimation of sulphanilamide gave low results when applied to sulphapyridine or sulphathiazole. In experiments on recovery of known amounts of the drugs added to blood, the values found ranged from 60% to 80% of the true figure. Marshall and Litchfield (1938) recommended destruction of excess nitrite with ammonium sulphamate. We used urea for destruction of nitrite; it improved the recovery of the drugs added to blood, but the results were still low. Buffering of the final mixture to pH 1·8 hastened the rate of colour development without altering the final reading. Finally, it was found that the recovery of the drugs added to blood was more satisfactory if the dilution of blood at the stage of protein precipitation was 1 : 20 instead of 1 : 10 as in the original method. Even in the method finally adopted the recovery of the drugs added to blood was only 90% of the true figure, but the loss was almost constant and the appropriate correction could therefore be made.

The series consisted of 30 cases of lobar pneumonia occurring between April, 1940, and January, 1941. There was no epidemic of pneumonia during the period, and the type of infecting pneumococcus varied so widely that nothing would be gained by describing the incidence of the different types. The ages of the patients ranged from 16 to 79. Alternate cases were treated with sulphathiazole and with sulphapyridine, without selection; 16 cases received sulphathiazole and 14 sulphapyridine. In the sulphathiazole group 11 patients were under the age of 30 and the eldest was 79; in the sulphapyridine group 10 were under 30 and the eldest was 58. In every case the free drug was given by mouth. Doses were given four-hourly. The standard dosage for sulphapyridine was 2 g. for the first three doses, then 1 g., continued until the temperature had definitely settled and the clinical condition was improving. The earlier cases treated with sulphathiazole received the same dosage as the group receiving sulphapyridine; later the dosage of sulphathiazole was doubled. The full dosage according to these three regimes was continued for periods ranging from 60 to 96 hours according to the clinical indications; in some cases treatment was continued at reduced dosage for a further period. Samples of blood for analysis were taken thrice daily at four-hourly intervals, the blood collections being made at the mid-point between doses of the drug.

CLINICAL RESULTS

Both drugs were effective in producing defervescence and clinical improvement. Apart from 3 cases with special complications, the time taken for the temperature to fall to normal was eight to fifty-six hours, and was usually within twenty-four hours. There was no significant difference in the rate of defervescence between the groups treated with the two drugs, and no apparent relation between the rate of defervescence and the concentration of the drug in the blood.

Of the patients treated with sulphathiazole, 1 died, a man of 79 who was gravely ill when treatment started. There was temporary improvement after one day of treatment, but he relapsed and died on the third day. There was one death also among the patients treated with sulphapyrdine, that of a man of 51.

Leucocyte counts were made daily in all cases and varied widely. In the group treated with sulphapyridine 12 showed a fall in leucocytes during treatment (maximum fall 23,400 cells per c.mm.), 3 showed no change and in 1 case there was a rise. In the group treated with sulphathiazole 9 cases showed a fall (maximum fall 23,000 cells per c.mm.), 3 showed no change and 4 showed small rises. There was no relation between the changes in the leucocyte count and the clinical course of the disease.

TABLE I—URINARY ABNORMALITIES IN PATIENTS TREATED WITH SULPHAPYRIDINE AND SULPHATHIAZOLE

—	Sulphapyridine	Sulphathiazole
Total cases	14	16
No. with urinary abnormalities	9	12
Albuminuria	8*	10
Gross hæmaturia	1	0
Microscopic findings:		
Red cells	5	3
Pus cells	3	6
Casts	3	2
Suppression of urine	0	1

* One patient had acute nephritis on admission.

The only toxic effects seen were vomiting and renal abnormalities. Vomiting was troublesome with both drugs, but was slightly commoner with sulphapyridine than with sulphathiazole; 10 out of 14 patients receiving sulphapyridine vomited, and 6 out of 16 receiving sulphathiazole. It should be noted, however, that 10 of the patients treated with sulphathiazole received double the dose used for the group on sulphapyridine, and 4 of the patients who vomited were on the higher dosage. It is difficult to say how far the renal abnormalities were due to treatment, since toxic damage to the kidney may occur in the untreated disease. The incidence of urinary changes is shown in table I.

BLOOD CONCENTRATIONS OF THE DRUGS

Results for 13 patients treated with sulphapyridine are shown in table II and fig. 1. There was a slight variation from the standard dosage in some cases; 7 received three initial doses of 2 g. followed by 1 g. four-hourly (fig. 1). Of the remainder, 4 had only two doses of 2 g. at the beginning, and 2 had four doses of 2 g. All are included in fig. 1, but the groups are separated in table II. The two lowest concentrations of the drug in the blood were found in patients who received only the two initial doses of 2 g., but apart from this the variations did not seem to be related to the intensity of the early dosage, and the group may therefore be considered as a whole. Individual variation in the concentrations reached with the same dosage was wide, but the characteristic result is a steep rise of the drug in the blood during the first twenty hours, and a more gradual rise later. Some cases showed a more or less steady plateau in this later period; only a few showed falling levels on a maintenance dose of 1 g. four-hourly. The results shown in table II and fig. 1

TABLE II—RESULTS IN 13 PATIENTS TREATED WITH SULPHAPYRIDINE

Drug	Dosage (g.)	Cases	Free drug in blood at: 18–22 hr.	42–46 hr.	66–70 hr.	90–94 hr.
			mg. per 100 c.cm.			
Sulphapyridine	221111..	4	2·4–10·3	4·6–12·6	4·4–16·0	
	222111..	7	6·1–15·3	11·5–13·5	10·0–20·7	8·0–15·5
	222211..	2	6·5–10·7	8·8– 9·4	8·1–11·2	9·4–18·0
	Mean of all cases	..	9·0	11·2	12·2	13·0
Sulphathiazole	222111..	(a) 1*	4·1–8·3	14·0	18·6	
		(b) 5	4·9–8·3	3·1–6·7	3·4–6·0	..
	Mean for group (b)	..	6·5	5·5	4·0	..
Sulphathiazole	444222..	10	6·3–15·5	5·5–11·5	3·0–12·0	..
	444422..	1	15·0	13·0	8·0	..
	Mean	..	8·5	8·1	7·8	..

* A fatal case (elderly patient).

refer only to the period during which the stated dosage was maintained, but further analyses were made after reduction of the dose in some cases. In these treatment was omitted during the night: this always resulted in a fall of the concentration of the drug in the blood.

The first 6 patients treated with sulphathiazole received three initial doses of 2 g. followed by 1 g. four-hourly, and the results in this group are therefore strictly comparable with those for the group treated with sulphapyridine. Of these 6 cases, 5 showed results which may be taken as characteristic (table II and fig. 2). The concentration of the drug in the blood rose during a period ranging from fourteen to thirty-four hours, reaching a peak of 5–9 mg. per 100 c.cm., and then gradually falling. The results are in striking contrast with those obtained for sulphapyridine; the maximum concentrations reached are lower, and with the maintenance dose of 1 g. four-hourly the blood sulphathiazole falls, whereas with the same dose of sulphapyridine the blood sulphapyridine usually continues to rise.

The sixth case in this group (the fatal case mentioned) shows a quite different result: the blood sulphathiazole rose rapidly and continuously, reaching 20 mg. per 100 c.cm. just before the patient's death. This accumulation of the drug in the blood may have been due to renal insufficiency, but we have no evidence on this point. It is impossible to say whether the high concentration of the drug in the blood contributed to the fatal result, or whether the accumulation of the drug was merely an incidental effect of the patient's condition.

When it became evident that the dosage of sulphathiazole used for these first 6 cases was not producing such high concentrations in the blood as were obtained with the same doses of sulphapyridine, it was decided to double the dosage for the remainder of the patients treated with sulphathiazole; 10 patients received the higher dosage, namely, three initial doses of 4 g. followed by 2 g. four-hourly (table II and fig. 3). There is great individual variation both in the maximum levels of the drug in the blood, and in the form of the curve obtained when the concentrations of the drug in the blood are plotted against the duration of treatment. The initial rise of the drug in the blood is steep; a peak is reached early, often in less than ten hours. After the early peak the level falls, usually quite steeply. Some cases show a secondary rise beginning after about thirty-eight hours of treatment. Although this group of patients received the higher dosage, they show distinctly lower levels of the drug in the blood than the patients receiving sulphapyridine in lower dosage, except in the earliest stage of the treatment. Moreover, the steady accumulation of the drug in the blood often found with a maintenance dose of 1 g. sulphapyridine four-hourly is not found with double the dose of sulphathiazole.

The results given in table II and fig. 3 are those found during the period of the standard dosage. In 7 of the cases further blood analyses were made after reduction of the dose, either by omission of the night doses (2 cases) or by reduction from 2 g. to 1 g. four-hourly. Reduction by either method caused a fall in the concentration of the drug in the blood; this confirmed the earlier observation that 1 g. of sulphathiazole four-hourly is not sufficient to maintain a steady level of the drug in the blood.

DISCUSSION

Like other workers, we have found great variation in the concentrations of free sulphapyridine or sulphathiazole in the blood of patients treated with the same drug in the same dosage. This is not surprising, as variations in the rate of absorption and excretion are to be expected in patients who are severely ill. But in spite of the individual variation, it has been shown that both sulphathiazole and sulphapyridine in the blood rise rapidly under the treatment to effective therapeutic levels, though these levels are much less readily maintained with sulphathiazole than with sulphapyridine. The curves shown (figs. 1–3) strongly suggest that sulphathiazole is absorbed as rapidly as sulphapyridine but is more rapidly excreted. We have made no analyses of the drugs in the urine in our cases, but the work of others has shown that sulphathiazole is more rapidly excreted than sulphapyridine both in animals (Van Dyke et al., 1939) and man (Spink and Hansen 1940, Strauss et al. 1941, Kinsman and Moore 1941).

Reports on the concentrations of sulphapyridine and sulphathiazole in the blood of patients under treatment have been made recently by others, and there are data available for large numbers of cases studied at different stages of treatment. On the whole the early period of treatment has been more fully studied than the later stages, and although all stages are represented there are not many records of the changes in concentration of the drug in the blood in the same patients throughout the treatment.

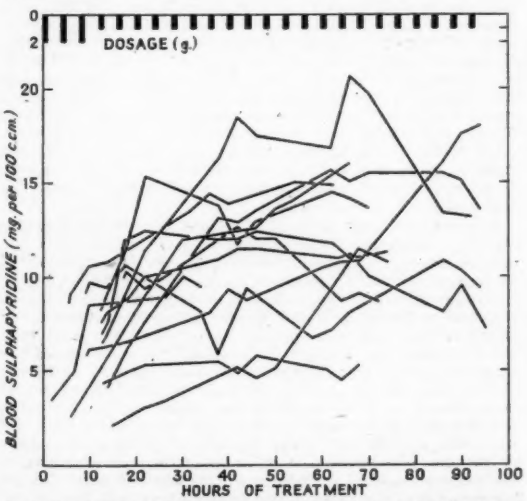

Fig. 1—Blood sulphapyridine during treatment; 7 patients received the dosage shown; 4 had 1 g. instead of 2 g. at the third dose; two had 2 g. instead of 1 g. at the fourth dose.

When the dosage is taken into account, the range of variation of the drug in the blood found in published studies is very similar to that recorded here. The figures of Kinsman and his colleagues (1939) for sulphapyridine are definitely lower on the average than ours. They used an initial dose of either 2 or 4 g. followed by 1 g. four-hourly, and the slightly lower initial dosage may partly explain their lower values for the drug in the blood. Also, their technical methods were likely to give rather low results.

Brown and his colleagues (1939) found, as we do, that with maintenance doses of 6 g. of sulphapyridine per day the level of the drug in the blood either rises or remains approximately steady. Barnett and his colleagues (1939), using doses of sulphapyridine higher than ours in relation to body-weight, reported either accumulation or steady maintenance of blood sulphapyridine. Volini and his colleagues (1940), comparing sulphapyridine with sulphathiazole at a dosage roughly the same as the lower dosage of our series, found, as we do, that the concentration of the drug in the blood is less well maintained with sulphathiazole than with sulphapyridine. A similar tendency to falling levels on a dose of 6 g. sulphathiazole daily is seen in the data of Sadusk and his colleagues (1940) and

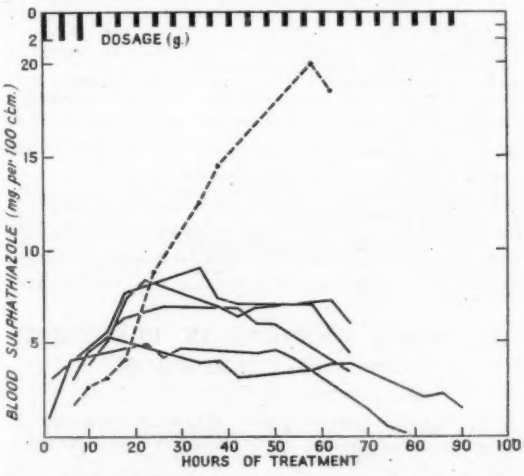

Fig. 2—Blood sulphathiazole during treatment. The dotted line shows the results for an old man who died.

Finland and his colleagues (1941), and the fact that the concentration of the drug in the blood is lower with sulphathiazole than with sulphapyridine is shown also in the results of Flippin and his colleagues (1941) and Kinsman and Moore (1941). Data for sulphapyridine only are also given by Cullen and Wilson (1940), Flippin and others (1939), Ratish and others (1940), Finland and others (1940), and Abernethy and others (1939); and for sulphathiazole only by Gaisford and Whitelaw (1940), Callomon and Goodpastor (1940) and Scott and Jones (1940).

In our series only the free drug in the blood has been estimated. As regards the bactericidal effect, only the free drug is concerned, but from the standpoint of toxicity the acetyl derivatives ("conjugated" drugs) ought also to be considered. It was shown by Marshall and his colleagues (1938) that the acetyl derivative of sulphapyridine is as toxic as the free drug. In the case of sulphapyridine, a large proportion of the total drug in the blood may be conjugated, and the conjugated form tends to accumulate with continued treatment (Brown et al. 1939, Ratish et al. 1940). Sulphathiazole is conjugated to a less degree than sulphapyridine in animals (Van Dyke et al. 1939, Long et al. 1940). The results of Sadusk and his colleagues (1940) and Strauss and his colleagues (1941) indicate the same in human subjects, but according to Flippin and his colleagues (1941) there is little difference between the two drugs on the average, though with sulphapyridine the proportion of the drug found in the conjugated form is more

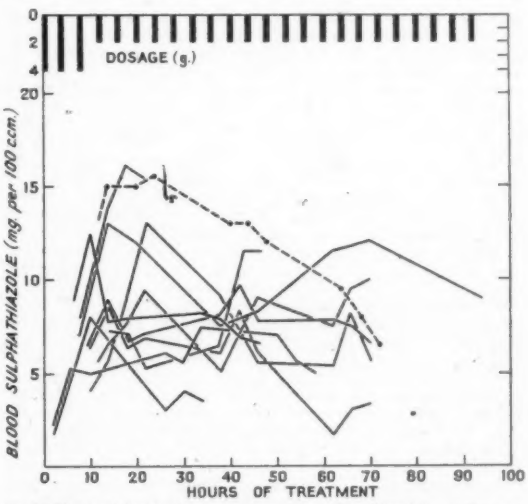

Fig. 3—Blood sulphathiazole during treatment. The dotted line refers to a patient who received 4 g. instead of 2 g. at the fourth dose.

variable than with sulphathiazole. Kinsman and Moore (1941) found a slightly greater degree of conjugation with sulphathiazole than with sulphapyridine, but in their results there was no undue accumulation of the acetyl derivative with either drug. On the whole, it seems that there is somewhat less risk of accumulation of the acetyl derivative when sulphathiazole is used.

As regards the bactericidal effect, Long and Bliss (1940) found that the action of sulphathiazole was equal to that of sulphapyridine at the same concentration when tested on the pneumococcus in vitro. It is difficult to determine with certainty what concentrations in the blood are required for the best therapeutic result. Most observers consider that 6 mg. per 100 c.cm. is adequate. We regularly obtained higher values than this by giving three initial doses of 2 g. sulphapyridine, followed by 1 g. four-hourly. With the same dose of sulphathiazole, 2 out of 6 cases failed to reach this level, and even in the group taking double the dose of sulphathiazole there were instances of failure to maintain a level of 6 mg. per 100 c.cm. or more consistently.

It is difficult to say whether it is an advantage to produce levels much above 6 mg. per 100 c.cm. In our short series of cases we found no correlation between the concentration of the drug in the blood and the rate of defervescence. Callomon and Goodpastor (1940) and Flippin and his colleagues (1941) studied larger numbers and also found no advantage from the higher concentrations. But this method of analysing the results is open to the objection that high blood levels are likely to be most frequent in patients with damaged kidneys, so that when the cases are classified according to the blood analyses the groups with higher figures are likely to include a higher proportion of patients gravely ill.

In comparing the clinical results with the two drugs, the best evidence is given by the work of those who have used both drugs over the same period, since the results are not then affected by variations in the severity of the disease in different epidemics. Such a comparison has been made by Volini and his colleagues (1940), who treated 164 patients with sulphapyridine and 169 with sulphathiazole; by Finland and his colleagues (1941), who treated 518 patients with sulphapyridine and 169 with sulphathiazole; by Flippin and his colleagues (1941), who treated 200 patients with sulphapyridine and 200 with sulphathiazole; and by Long and Haviland (1940). In these studies there was some difference in the intensity of the initial dosage; the total dose in the first 24 hours ranged from 7 to 12 g., but all used a maintenance dose of 1 g. four-hourly in the succeeding period. Under these conditions there was no significant difference between the two drugs as judged by mortality rates. Flippin and his colleagues reported more rapid defervescence with sulphapyridine than with sulpha-

thiazole. Garvin (1940) also compared the two drugs, treating 40 patients with sulphathiazole and 62 with sulphapyridine. He recognised that it was necessary to use a higher dosage of sulphathiazole than of sulphapyridine in order to get approximately comparable concentrations of the drug in the blood. For sulphapyridine he used one initial dose of 2 g. followed by 1 g. four-hourly, and for sulphathiazole one initial dose of 4 g. followed by 2 g. four-hourly. There was no significant difference in the fatality-rates in the two groups, but there was more rapid defervescence with sulphapyridine than with sulphathiazole. Wagoner and Hunting (1941) used sulphapyridine and sulphathiazole in the treatment of pneumonia in children. They aimed at a concentration of 4–6 mg. per 100 c.cm in the blood, adjusting the dosage as required. The two drugs were equally effective.

Evidence of the incidence of toxic effects for both sulphapyridine and sulphathiazole has been given by Flippin and his colleagues (1940, 1941), Finland and his colleagues (1941), Garvin (1940), Wagoner and Hunting (1941), and Kinsman and Moore (1941). For sulphapyridine only, the toxic effects are analysed also by Finland and his colleagues (1940), and for sulphathiazole only by Volini and his colleagues (1940), Reinhold and his colleagues (1940), Pepper and Ham (1940), Spink and Hansen (1940), Scott and Jones (1940), and Callomon and Goodpastor (1940). Taking all these results together, the most striking difference is the much greater incidence of nausea and vomiting with sulphapyridine. The rarer toxic effects—damage to the kidneys, damage to the hæmopoietic tissues, drug rashes, drug fever and mental symptoms—are all slightly commoner with sulphapyridine than with sulphathiazole. However, most of these observers used the two drugs at approximately the same dosage, so that the average concentration of the drug in the blood would be lower in the groups treated with sulphathiazole. Garvin's series, in which the dosage of sulphathiazole was double that of sulphapyridine, also showed a higher incidence and greater severity of vomiting with sulphapyridine than sulphathiazole. There was little difference in the incidence of dermatitis (though there were too few cases of dermatitis in either group for a true comparison). Crystals of the drug in the urine were found much more often with sulphathiazole than with sulphapyridine, and microscopic hæmaturia was rather commoner with sulphathiazole. Wagoner and Hunting (1941) found vomiting commoner with sulphapyridine than sulphathiazole, although they adjusted their dosage to get similar concentrations of the drugs in the blood.

In conclusion, it is evident that in order to get the same concentration of the drug in the blood, sulphathiazole must be used in much higher dosage than sulphapyridine. With sulphathiazole, the maintenance of an effective blood level is more difficult, and it depends on a balance whereby greater amounts are absorbed and excreted than with sulphapyridine; hence there may be a greater danger of crystallisation of the drug in the kidneys when sulphathiazole is used. Also, it becomes more important to check the progress of the treatment by blood analyses when sulphathiazole is used, in order to avoid excessive retention of the drug if the kidneys are damaged. The only advantage of sulphathiazole seems to be a less tendency to cause vomiting, but even this advantage is less striking in the experience of workers who increased the dosage of sulphathiazole in order to compensate for its more rapid excretion.

SUMMARY

Sulphapyridine has been compared with sulphathiazole in the treatment of 30 cases of lobar pneumonia.

The concentrations of free sulphapyridine and free sulphathiazole in the blood of the patients have been followed throughout the course of treatment.

Effective concentrations of the drug in the blood are much more readily maintained with sulphapyridine than with sulphathiazole, and this is explained by the more rapid excretion of sulphathiazole.

The present series is too short for an adequate evaluation of clinical results, but recent reports on much larger numbers are reviewed, and it is concluded that sulphathiazole has no advantage over sulphapyridine as a chemotherapeutic agent. Sulphathiazole has less tendency to cause vomiting.

We wish to thank Dr. J. A. Charles, medical officer of health to Newcastle-on-Tyne, for giving us the opportunity to investigate patients at the Newcastle General Hospital and the City Hospital for Infectious Diseases, and Messrs. May and Baker for supplies of sulphapyridine ('M & B 693') and sulphathiazole ('M & B 760').

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THE GRAVE ANÆMIAS IN PREGNANCY AND THE PUERPERIUM

REPORT OF 17 CASES

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IN the last few years an increasing number of cases of grave anæmia of pregnancy have been reported, but the condition is uncommon. Full reviews of this subject have been given by Wilkinson (1932), Whitby (1932), Witts (1932), and by Stevenson (1938), who, during 1928–34, studied 30 cases, the largest number reported by any one observer.

During 1934–41 I have studied and followed up 17 patients suffering from grave anæmias of pregnancy. These fall into two groups: cases 1–9 are of the pernicious variety; cases 10–17 belong to the hæmolytic group. In each patient a critical search was made to exclude infection, carditis, nephritis and other diseases which could possibly have been factors in the production of a severe anæmia.

Temporary Pernicious Anæmia of Pregnancy

In order to save space, only positive clinical findings are given. Intermediate blood and other reports are omitted. Fresh blood was used for all transfusions, from donors of the same group as the patients; cross-matching was performed in every case. No difficulty was experienced in grouping. The blood was always given slowly by the drip method, and no abnormal reaction ever followed.

CASE 1.—Age 31. Two former pregnancies. Pyelitis during the first; second normal. Otherwise healthy. In May, 1933, she again became pregnant. Much vomiting. November, premature delivery of stillborn twins. No undue hæmorrhage or other complications. Since then increasing weakness, breathlessness and pallor. On admission to hospital on May 14, 1934, she was very ill. Slight lemon-yellow tinge of skin; glossitis; spleen palpable. Red cells

1,960,000; Hb. 50%; colour-index 1·3; white cells 11,200; normal differential count; red cells irregular in shape and size; normoblasts numerous, with some megaloblasts, myeloblasts and punctate basophilia; reticulocytes under 1% of red cells. Free acid in normal amount in gastric juice. Pyrexia continued for a few days. Given diet rich in protein, with half a pound of liver each day; and 'Ventriculin' (PDCo) 1 vial t.d.s. She improved very much both clinically and hæmatologically, and by the following August felt quite well and had a normal blood-count. All specific treatment was discontinued.

She has been seen from time to time (last, in September, 1941), and has kept well with a normal blood-count. No further pregnancy.

CASE 2.—Age 27. A hawker. Always healthy. Three normal pregnancies and confinements. Fourth child born on May 18, 1934; well during this pregnancy. No antenatal care; normal confinement: no undue blood loss. Pallor noticed directly after confinement. On admission to hospital on the same day she was extremely ill with well-marked pallor and pyrexia. Red cells 925,000; Hb. 30%; CI 1·16; halo 8·19 μ; white cells 10,400; normal differential count; red cells irregular in shape and size; megaloblasts and many normoblasts seen; reticulocytes under 1%. Free acid in gastric juice was below normal. Well-marked periostitis of the tibiæ; Wassermann and Kahn reactions strongly positive. 'Hepatex' (Evans) 5 c.cm. given intramuscularly each day for a week and then hog's stomach 2 dr. t.d.s. Pyrexia disappeared; blood value quickly increased. All specific treatment was then discontinued.

In August, 1941, she replied to a questionnaire that both she and the child had been quite well since she left hospital; she had had no further pregnancies. She did not submit to antisyphilitic treatment which was advised.

CASE 3.—Age 37. Had had 5 children; normal pregnancies and confinements. Health always good. Last child born July 16, 1935. Some swelling of feet during last three months of this pregnancy. Had antenatal care. No undue blood loss. Since confinement, increasing weakness, breathlessness, swelling of feet, pallor and soreness of tongue. Admitted to hospital Oct. 23, 1935, extremely ill. Very pale with slight icteric tinge of the skin; much glossitis; numbness and paræsthesia of forearms and hands, but nothing objective found in the rest of the nervous system, except retinal hæmorrhages. Spleen just palpable. Red cells 750,000; Hb. 19%; CI 1·2; white cells 5600; normal differential count; many nucleated red cells, considerable anisocytosis, poikilocytosis and polychromasia; reticulocytes under 1% of the red cells. Complete absence of free acid from gastric juice. Child healthy with no sign of anæmia. Patient was transfused, and hepatex (2 c.cm.) was injected intramuscularly each day. Good reticulocyte response. Patient's condition began to improve and temperature to settle; in a month's time blood-count had become normal. A second test-meal showed a normal amount of free acid. Specific treatment discontinued.

Both she and the child remained well. In 1936 she again became pregnant. She remained well with a normal blood-count; hepatex, 2 c.cm., was given once every two weeks as a prophylactic. In October she was delivered of a healthy child; normal pregnancy and puerperium. Another child was born in 1940 with no ill effect on her health. No specific treatment given during this pregnancy. Last seen in 1941; health then good and blood still normal.

CASE 4.—Age 33. Health had always been good. First child born Dec. 31, 1934. Healthy pregnancy with antenatal care and a normal confinement. Afterwards she was weak and pale, with shortness of breath and lemon coloration of the skin. On admission to hospital on Feb. 4, 1935, she was very ill, with high pyrexia. Petechial hæmorrhages into the skin, hæmorrhages into both retinæ, and glossitis. Red cells 730,000; Hb. 24%; CI 1·6; halo 7·6 μ; white cells 6400; differential count normal; red cells very irregular in shape and size, with polychromasia and megalocytosis; reticulocytes 1·5% of the red cells; platelets 80,000; fragility of red cells not increased. Van den Bergh reaction was practically negative. No free acid found in gastric juice. Hepatex, 5 c.cm., at first intravenously and then intramuscularly, given each day. Brisk reticulocyte response. General condition improved and by the end of March, when she left hospital, blood was normal. A test-meal showed normal acidity. The baby was healthy.

Her doctor reported in September, 1941, that she had remained well without any specific treatment. No further pregnancy.

CASE 5.—Age 32. Had always been healthy. Normal pregnancy and puerperium with the first child. Second child born April 6, 1937. During the last weeks of this pregnancy pale with increasing weakness and shortness of breath; much vomiting and taking little food. On admission to hospital on April 10 she was extremely ill. Red cells 1,150,000; Hb. 23%; CI 1·1; halo 7·4 μ; white cells 12,000; normal differential count; red cells irregular in shape and size, with 400 normoblasts per c.mm., and punctate basophilia; reticulocytes under 1%. Van den Bergh test gave a faintly positive indirect reaction. Small amount of free acid in gastric juice. Two blood-transfusions given at short intervals, and hepatex, 4 c.cm., injected each day. By the end of July blood was normal. All specific treatment then discontinued. Child healthy.

Since then the patient has remained well with a normal blood-count. No further pregnancy.

CASE 6.—Age 33. Had always been well. Normal first pregnancy until the last two months, when she began to be short of breath. Normal confinement on Dec. 16, 1938. No undue loss of blood. Manual removal of placenta. Increased pallor and pyrexia after delivery. On admission: red cells 2,000,000; Hb. 42%; CI 0·91; white cells 6300; differential count normal; poikilocytosis, anisocytosis, normoblasts and megaloblasts seen; reticulocytes under 1%. Test-meal showed free acid though in diminished amounts. Child was healthy. Hepatex, 4 c.cm., given each day intramuscularly; satisfactory reticulocyte response. Blood-count rose to full value. Specific treatment then discontinued.

She has remained well with a normal blood-count. No further pregnancy.

CASE 7.—Age 31. First child, normal pregnancy and puerperium. Good health until the second pregnancy. Husband out of work; food at home, especially meat, had been short. For the last two months of the pregnancy she had been short of breath, weak and pale, and was treated for toxæmia of pregnancy by being kept in bed on a milk diet. Normal confinement on May 1, 1941. Then condition suddenly became worse. Faint icteric tinge of the skin. Red cells 650,000; Hb. 24%; CI 1·8; white cells 6500; halo 7·8 μ; poikilocytosis, polychromasia and anisocytosis; normoblasts 180 per c.mm.; reticulocytes 1% of red cells. Test-meal showed free acid but in diminished amount. Hepatex, 4 c.cm., given intramuscularly each day. Satisfactory reticulocyte response. Blood value rose and general condition improved. Specific treatment then discontinued.

When last seen in September, 1941, she had been well since leaving hospital. No further pregnancy. Child had remained well.

CASE 8.—Age 29. Five normal pregnancies. Had always been well. Became pregnant again in May, 1941. After the first month undue tiredness and lack of energy. Miscarriage on Sept. 4; no undue hæmorrhage. Became very pale and short of breath directly afterwards. Red cells 2,100,000; Hb. 45%; CI 1·09; white cells 5300; normal differential count; well-marked anisocytosis and poikilocytosis; normoblasts 100 per c.mm.; reticulocytes under 2%; platelets diminished. Test-meal showed normal acidity. Brisk reticulocyte response followed daily injections of 4 c.cm. of hepatex. Rapidly improved. When her blood-count became normal specific treatment was discontinued. She remains well.

CASE 9.—Age 28. Had always been well until the last two months of the second pregnancy, when the legs swelled and she became somewhat weak and pale. Normal confinement on Aug. 30, 1941. No undue blood loss. Child healthy. Admitted to hospital a month later as symptoms had become worse. Glossitis and well-marked retinal hæmorrhages. Red cells 2,100,000; Hb. 40%; CI 0·95; white cells 5300; normal differential count; anisocytosis and poikilocytosis; normoblasts 50 per c.mm.; platelets diminished. Biopsy of bone-marrow showed increased cellularity with megaloblastic hyperplasia. Acid in gastric juice below normal. Hepatex, 4 c.cm., injected intramuscularly each day. Brisk reticulocyte response followed. Improved clinically and hæmatologically. By November the blood was normal and specific treatment was discontinued. A second test-meal showed a normal amount of acid. She remains well.

COMMENT

Pernicious anæmia of pregnancy usually occurs in multiparæ, generally in the middle or later years of

reproductive life. In this series the average age was 31 years. The early signs are often insidious, appearing usually during the last three months of pregnancy; they may easily be missed. Some patients go through pregnancy without serious inconvenience. In others, the anæmia develops suddenly, often dramatically, soon after delivery (cases 2, 3, 4 and 6). The symptoms, signs and changes in the blood are similar to those found in Addison's anæmia. In the pernicious anæmia of pregnancy, however, the mean diameter of the red cells may approach more to normal, and there is as a rule no leucopenia. There are no signs of hæmolysis. The bone-marrow is similar in both diseases; but in pernicious anæmia of pregnancy, unlike Addison's anæmia, no organic lesions of the brain or spinal cord have been reported except in one case (Strauss and Castle 1933), though mild paræsthesias are occasionally found (case 3). Severe antepartum or postpartum hæmorrhage and sepsis are as a rule remarkable by their absence.

The similarity of Addison's anæmia to this temporary pernicious type and the fact that in the latter there is often a derangement of gastric function, shown by the diminution or absence of hydrochloric acid in the test-meal, suggest that an analogous mechanism is likely to be involved (Strauss and Castle 1933). In the cases reported here, hydrochloric acid was found in normal amounts in only 2; in 2 it was absent and in 5 deficient in amount. Deficiency of extrinsic factor in the diet might have been responsible, at any rate partially, for the anæmia in some patients (cases 1, 5 and 7). After delivery the level of the acid may rise to normal (cases 3, 4 and 9).

Acute Hæmolytic Anæmia of Pregnancy

The following 8 patients were found to be suffering from acute hæmolytic anæmia, of the type described by Lederer (1930).

CASE 10.—Age 28. Shortness of breath and unusual pallor towards end of first pregnancy. Normal confinement on May 12, 1939. Child healthy. No undue blood loss. Symptoms became worse in spite of treatment with liver and iron. Admitted to hospital on July 7. Very ill with pyrexia, icteric tinge of the skin and glazing of the tongue. Red cells 1,500,000; Hb. 35%; CI 1·2; halo 7·6 μ; red cells irregular in shape and size with many normoblasts and megaloblasts; reticulocytes 10% of red-cells; platelets not reduced. Strongly positive indirect van den Bergh reaction. Normal acid in gastric juice. A course of hepatex, 4 c.cm., intramuscularly each day and several blood-transfusions given. Condition improved and pyrexia disappeared. Blood value rose to normal.

When last seen in September, 1941, her health had remained good. There had been no further pregnancy.

CASE 11.—Age 30. Three children. Pregnancies and confinements normal. Health good until pleurisy during the seventh month of the fourth pregnancy. Progressive weakness, pallor and shortness of breath since. Normal confinement on Nov. 25, 1938. Child healthy. In spite of repeated injections of liver her condition deteriorated, and she was admitted to hospital on Feb. 3, 1939, extremely ill. Red cells 1,200,000; Hb. 20%; CI 0·83; poikilocytosis, anisocytosis and polychromasia well-marked; megaloblasts and normoblasts present; reticulocytes 15% of red cells; mean corpuscular thickness normal; no spherocytes seen; fragility of red cells slightly increased. Indirect van den Bergh reaction present. Test-meal showed no free acid. Three blood-transfusions given, with liver extract and iron. A month later her condition had vastly improved. Red cells 3,500,000; Hb. 70%; no immature cells seen.

She has remained well with a normal blood-count and without any specific treatment. No further pregnancies.

CASE 12.—Age 35. Normal first pregnancy and confinement on Feb. 16, 1939. No antenatal care. No undue blood loss. Since then, pale, weak and short of breath, with pyrexia and an icteric colour. Red cells 1,200,000; Hb. 25%; CI 1·04; halo 7·6 μ; white cells 13,000; normal differential count; well-marked anisocytosis, poikilocytosis and polychromasia; normoblasts, stippling of red cells and myelocytes; reticulocytes 20% of red cells; platelets 250,000; fragility of red cells normal. Hydrochloric acid in normal quantities in the test-meal. She improved after treatment with several blood-transfusions. Pyrexia diminished; blood increased in value and reticulocyte count diminished. The child remained well.

In September, 1941, she replied to a questionnaire that her health had remained good. Another healthy child was born in June, 1941. No antenatal care. Normal pregnancy and confinement.

CASE 13.—Age 35. Second child born Nov. 29, 1938. Normal pregnancies and confinements. No undue blood loss. No antenatal care. Lost energy and became short of breath and increasingly pale directly after the second confinement. Treated with large doses of liver, iron, vitamin C and a generous diet. No improvement. Admitted to hospital on June 29, 1939. Red cells 1,390,000; Hb. 40%; CI 1·4; halo 8·3 μ; white cells 4000 with a normal differential count; red cells irregular in shape and size, with many normoblasts and megaloblasts; reticulocytes 15% of red cells; platelets 405,000; strong indirect van den Bergh reaction. Normal amount of free acid in gastric juice. Several blood-transfusions given. She left hospital well with a normal blood-count.

In September, 1941, she replied to a questionnaire that she and the child had remained well. No further pregnancy.

CASE 14.—Age 20. Health good until a miscarriage in June, 1939, when three months pregnant. No serious hæmorrhage. Admitted to hospital a week later on account of abdominal pain and pyrexia. A mass felt in the left fornix. Normal red-cell count with a leucocytosis of 21,000 per c.mm. Cultures from the cervix gave a growth of hæmolytic streptococci, but blood cultures made under aerobic and anaerobic conditions remained sterile. The uterus was explored and she was given sulphanilamide, 1 g. 4-hourly for a week, and nursed in the fresh air. Her condition deteriorated; blood-count started to fall and jaundice developed. On July 30, red cells 1,340,000; Hb. 37%; CI 1·4; halo 8·6 μ; red cells irregular in shape and size; normoblasts 2500 per c.mm.; megaloblasts present; reticulocytes 25% of the red cells; no spherocytosis or ghost cells seen. Van den Bergh test showed a strongly positive indirect reaction. Urine contained albumin and urobilin. Liver and spleen enlarged. Treated with blood-transfusions, liver extract and iron. Improvement and relapses followed. In October she left hospital much improved, with a normal blood-count.

In September, 1941, in answer to a questionnaire, she replied that she had quickly regained her health after leaving hospital and had remained well. No further pregnancy.

CASE 15.—Age 29. Health had always been good. Periods regular, the last being four weeks before admission. On Feb. 1, 1940, excessive vaginal hæmorrhage. Rapidly became pale and jaundiced. She lived in an isolated farm and owing to the depth of snowdrifts the doctor, after several attempts, could only reach her at the end of the second day. With the greatest difficulty she was removed to hospital the next day and arrived in a state of extreme shock. All bleeding had stopped. Pallor and jaundice were severe, and in spite of resuscitation, including a blood-transfusion, she died within a short time of admission. A blood examination made shortly before death showed red cells 1,260,000; Hb. 36%; CI 1·4; halo 8·0 μ; white cells 64,000; many normoblasts and megaloblasts; reticulocytes 30% of the red cells; platelets normal. Strong indirect van den Bergh reaction.

At autopsy the spleen was typical, histologically, of the kind seen in hæmolytic anæmia (Lescher and Osborn 1939); gross engorgement of the sinusoids; blood-cells were being rapidly destroyed by the littoral cells; abundant hæmosiderin granules. Bone-marrow deep red and cellular; normoblasts predominated, though all the series were represented. Acini and ducts of the breasts were distended with milk. The cervix admitted the tip of the little finger. No trace of placental elements found.

CASE 16.—Age 24. Normal first pregnancy and confinement Jan. 20, 1941. No undue hæmorrhage. Child healthy. Patient became pale and breathless soon after delivery; anæmic and jaundiced. Pelvic cellulitis with swelling of the right leg. Red cells 3,000,000; Hb. 53%; CI 0·88; halo 7·8 μ; white cells 21,400; megalocytosis, anisocytosis and poikilocytosis; normoblasts 200 per c.mm., with numerous reticulocytes; mean corpuscular thickness and volume increased. Strongly positive indirect van den Bergh reaction. Smears from cervix showed streptococci, but there was no growth. Blood-cultures negative. Sulphanilamide treatment was started and she was given two blood-transfusions. In a fortnight she began to improve and the temperature fell. She left hospital on March 3, much better, with an almost normal blood-count. The child was well.

When last seen in September, 1941, her health had remained good and there was no anæmia. No further pregnancy.

CASE 17.—Age 34. Had always been well. First pregnancy and confinement on Feb. 22, 1941, was normal. Directly afterwards she became weak, short of breath and pale, with an icteric tinge. Red cells 500,000; Hb. 30%; CI 1·0; halo 8·0 μ; poikilocytosis and polychromasia; normoblasts 230 per c.mm.; reticulocytes 12%; platelets not reduced; fragility of red cells normal. Strongly positive indirect van den Bergh reaction. Injections of liver extract given each day. She improved and left hospital with red cells 3,750,000; Hb. 60%; white cells 5800; no abnormal red cells; reticulocytes 4%. The child was well.

No reply was received to a questionnaire sent in September, 1941.

COMMENT

It has already been pointed out (Lescher and Osborn 1939) that the hæmolytic anæmias form a somewhat unsatisfactory group, since there is actually no very clear and accepted standard as to what constitutes clinical hæmolysis. Even when its existence is accepted there is seldom direct evidence of it (such as hæmoglobinæmia, hæmosiderinuria and the presence of ghost cases) since it occurs rarely in the blood-stream itself. Acute hæmolytic anæmia occurs, of course, in conditions other than pregnancy. There is no evidence that a hæmolysin ever develops in the maternal or fœtal structures. Neither nutritional and digestive defects nor infection seem to play any part in its production.

Prognosis, Treatment and Differentiation

Patients with these grave anæmias of pregnancy should not be allowed to drift in the hope of spontaneous cure; for the old belief that a cure results after delivery without specific treatment, is without foundation. For example, cases 1, 10, 12, and 13 were very ill for some months after confinement, and no improvement took place until specific treatment was started. Before the renaissance in the treatment of Addison's anæmia the maternal mortality of patients suffering from temporary pernicious anæmia of pregnancy was high, and so was the fœtal death-rate. Now, with accurate diagnosis and adequate treatment, the prognosis has much improved. In the 9 cases reported here the maternal death-rate was nil. In cases 1 and 8 the children were stillborn. There is no reliable evidence that the children inherit either type of anæmia.

Temporary pernicious anæmia of pregnancy will respond well to adequate treatment with liver preparations, although Davidson has called attention to similar cases who were refractory to this treatment; and there is a reasonable chance of the patient bearing a healthy child. This treatment should be continued until the blood is normal and the pregnancy over, after which it can be discontinued, since in this type of anæmia, unlike Addison's anæmia, relapses will not occur. If the anæmia is due to the absence from the diet of extrinsic factor (as it may have been in cases 1, 5 and 7), the addition of meat protein or 'Marmite' to the diet, or treatment with liver, should bring about improvement. Blood-transfusions were resorted to as an emergency measure in cases 3 and 5, because these patients were very ill; but with a better knowledge of the efficiency of liver treatment these may have been unnecessary.

While the ætiology of Lederer's anæmia remains unknown, treatment must necessarily be empirical. Patients often react dramatically, especially after parturition, to a blood-transfusion, repeated if necessary. Even though some of these patients were desperately ill, they all recovered with the exception of one (case 15), and she was moribund on admission to hospital. Case 14 did not respond quickly, possibly because of the coincident sepsis. It is true that liver and iron were given to several of the patients reported above, together with blood-transfusions. But in cases 10, 11 and 13 liver and iron and a generous diet were used for several months with no improvement until treatment with blood-transfusions was started; in case 17, it is true, recovery followed the use of liver alone.

Patients suffering from either of these grave anæmias, when treated promptly and energetically, may be allowed to go to term, and there is a reasonable chance of the patient bearing a healthy child. A critical review of published work supports, on the whole, the view that these anæmias, especially the pernicious variety, may recur in subsequent pregnancies, but with suitable antenatal supervision, including blood-examinations, the necessary treatment can be given early, so that these patients should be able to complete their pregnancies successfully. In this series only 2 patients became pregnant subsequently. There was no return of the anæmia.

From the history and clinical signs alone a differential diagnosis cannot be made with certainty between temporary pernicious anæmia and hæmolytic anæmia, save that in most cases of the hæmolytic type in the above series the patient had an icteric colour as compared with the slightly lemon tinge seen in the patients with pernicious anæmia. Glossitis was found in 4 of the temporary pernicious anæmia cases, whereas it occurred in only 1 suffering from the hæmolytic type. With both varieties the anæmia was severe, and most of the cases were of the megalocytic type. The red cells showed considerable irregularity in size and shape, with normoblasts and occasionally punctate basophilia. Megaloblasts were rather more prominent in the hæmolytic type. No spherocytosis was seen. Estimation of the fragility of the red cells was of no help.

The main differentiating points found in the blood examinations were three. First, in the hæmolytic type of anæmia not under specific treatment, the percentage of reticulocytes was always much raised; this was so in every case in the series. In temporary pernicious anæmia, however, these cells were not increased unless liver had been given recently, and even then the rise was not sustained for longer than a few days; all the cases of temporary pernicious anæmia in which this test was tried gave a typical reticulocyte response followed by a rise in the number of the red cells. Secondly, in temporary pernicious anæmia the serum bilirubin is within normal limits or only slightly raised, and there is only a faint indirect van den Bergh reaction. In the hæmolytic type, however, since the anæmia is caused by hæmolysis of the red cells with the liberation of hæmoglobin, the serum bilirubin is naturally increased and there is a strongly positive indirect van den Bergh reaction. Had more samples of bone-marrow been obtained, by sternal puncture, they would no doubt have provided information useful in differentiating these two types of anæmia. One would have expected, in the pernicious type, a mixed erythroblastic reaction with great increase in the number of megaloblasts; whereas in hæmolytic anæmia, although there are signs of great marrow activity, the hyperplasia is normoblastic in type (cases 9 and 15). Thirdly, the two varieties of anæmia react differently to specific remedies: liver extract given parentally in large doses will raise the level of the blood to normal in temporary pernicious anæmia; but it will not have this effect in the hæmolytic type occurring during pregnancy—for such cases blood-transfusions are necessary.

SUMMARY

A series of 17 cases of grave anæmia associated with pregnancy has been reported; 9 with temporary pernicious anæmia and 8 hæmolytic anæmia (Lederer).

In 8 cases the symptoms and signs of the anæmia started before delivery, generally in the last 3 months of pregnancy, and progressed, generally rapidly, after parturition. In the remainder the anæmia developed suddenly, often dramatically, after the confinement.

No patient had received adequate antenatal supervision and treatment. No blood-examinations had been made before admission to hospital; increased facilities for blood-examinations during pregnancy are needed.

It is important to determine the type of anæmia before beginning treatment. There is a specific treatment for each of the types of anæmia described, which if given early should much reduce the maternal and fœtal mortality.

With adequate antenatal supervision, including blood-examinations, a woman who has previously suffered from one of these grave anæmias should be able to undergo subsequent pregnancies successfully.

My thanks are due to Mr. N. Edwards for permission to study several of the patients who were admitted under his care.

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ELECTRICAL CONVULSION THERAPY

CLINICAL OBSERVATIONS

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SINCE the introduction into this country, more than two years ago, of electrically induced convulsion therapy the method has gained fairly wide acceptance, and enough cases have been treated to allow of discussion of its merits or otherwise, and of the types of disorders for which it is especially applicable.

A series of 200 cases (63 in males and 137 in females) of both acute and chronic mental illnesses, in whom treatment has been completed for not less than three months, provides the material for this paper. All were inpatients of the Bristol Mental Hospital, but conclusions will be based on additional experience gained in treating others, as well as on the cases in the series.

METHOD

The instrument used was a standard machine * in which time can be varied by 0·05 sec. and voltage up to 150 volts; the voltage variations are represented by a scale graduated from 0 to 100, and the makers supply a graph on which the real values of these calibrations can be read. The general principles and technique have been described elsewhere (Kalinowsky 1939, Fleming et al. 1939, Shepley and McGregor 1939, Hemphill and Walter 1941, Androp 1941a) and no important modification suggested itself. As a routine, the labyrinth was stimulated by syringing the ear with cold water before inducing the fit. This seems to facilitate the return of breathing after the fit.

In order to establish a standard and convenient practice, after experimenting with various combinations of voltage and time, in more recent patients the initial time has been set for 0·2 sec., and the voltage increased from the 20th calibration by steps of 20% up to the maximum, if necessary, until a fit results. If still ineffective the time alone is increased by 0·05 sec., up to 0·6 sec. On the whole, settings of the maximum voltage with durations of not more than 0·3 sec. have been adequate for most patients. Young males almost invariably have a lower threshold, and in treating these the time is set at first at 0·15 sec. In many subjects there is a slight increase in the threshold during the first three or four fits (Kalinowsky et al. 1941) which usually remains steady thereafter. In a small number of cases the threshold increases after each fit, so that eventually it may be impossible consistently to produce a major convulsion with the maximum voltage and what may be considered the maximum duration of current permissible—namely, 0·6 sec. This peculiarity was only observed in women, and it appeared to be a bad prognostic sign. It occurred in the rare cases of depression which failed to improve and in one case of hysteria as well as in certain of the schizophrenic group.

FRACTURES AND PHYSICAL MISHAPS

The danger of fractures of various bones in shock treatment has attracted attention out of all proportion to its importance, and my experience has not justified experiments with curare and similar drugs recently in vogue (Harris et al. 1941). In all patients treated, including many not reviewed here, fractures were noted in 3: compression fractures of the bodies of some dorsal vertebræ in one woman who had sustained an injury of the same sort 14 months before admission to hospital; fracture of the surgical neck of the humerus in a man aged 52; and an extracapsular fracture of the neck of the femur in a physically healthy muscular man of 26. Both fractures of the long bones were noticed as the patient recovered from the fit and could only be explained as the result of violent muscular action. Neither the positioning nor the convulsion were in any way unusual in either case. Fractures of the humerus have been reported (Gonda 1941, Bingel and Meggendorfer 1940), but to my knowledge no fractured femur has been reported before, although bilateral fracture of the femoral necks has occurred in pharmacological convulsions (Androp 1941b).

Physical illness, sepsis or a prophylactic inoculation within 48 hours of treatment are contra-indications. In spite of careful investigation of the physical state, the treatment may have been to some extent responsible for subsequent illness in a small number of cases. In 2 apparently healthy patients clinical signs of active pulmonary tuberculosis developed before the third week of treatment, and both died within the next six months, one of miliary tuberculosis with tubercles in most organs including the meninges. Autopsy showed evidence of old tubercular foci in the lungs of each, with extensive spread of recent origin. It is likely that the violent movements and postconvulsive hyperventilation broke down fibrous barriers thereby activating latent tuberculosis. In one young man an extensive tubercular adenitis of the neck developed rapidly after the fourth convulsion. In 2 cases recovery from each fit was slow, the pulse being feeble and heart sounds almost imperceptible, and was followed by persistent cardiac arrythmia. Although these symptoms disappeared in the course of a week further treatment was deemed inadvisable.

DURATION OF TREATMENT

Opinion differs as to how often fits should be induced, or what constitutes a course of treatment. Three methods have been tried: 3 fits weekly, 2 fits weekly, and daily fits for two or more weeks. In each case treatment was terminated gradually by 3 or 4 fits each at weekly intervals.

The first method seems to be satisfactory for serious psychoses and I find it the method of choice for many such cases. In milder illnesses, or where considerable improvement takes place after one fit, it has the disadvantage that the patient seems to become excessively dependent on the treatment and that single day intervals are not long enough to allow a good contact to be made with the outer world—as if the treatment was breaking the continuity of normal life rather than of the psychosis. In mild cases of the manic-depressive and psychoneurotic types relapses have been seen when the interval between fits was increased to a week, a disadvantage not encountered so often when only 2 fits per week are tried for two weeks, with increase if there is no improvement. Every effort is made to occupy the patient and to get him to take his place in the normal world from the very beginning. Relatives are encouraged to visit frequently and take the patient for outings or home for week-ends. He is protected as far as is practicable from contact with other patients who freely express psychotic ideas. If no improvement has resulted by the 9th fit no further fits are induced: recoverable cases have usually shown improvement before the 5th fit.

The daily method was tried in 2 cases of mania and 2 of depression as well as in a number of chronic schizophrenics. The manics and depressives relapsed, eventually to recover. In both depressives a phase of restless confusion developed and endured for several days. After its subsidence psychotic symptoms disappeared. The picture in both was rather like postepileptic irritability with confusion and aimlessly violent behaviour. There has been a complete and lasting amnesia in both for this phase.

In the schizophrenics daily fits were induced for upwards of 30 days. No beneficial effect was observed at the time, some being more confused and uncoöperative, but in subsequent weeks several patients showed more sociable conduct, became clearer and could be employed. They have not relapsed. In some there was a loss of weight and physical deterioration after the first week. This was attributed to inadequate nourishment; these chronic patients came from large refractory wards where they could not possibly receive individual supervision at meal times. After induced fits they were sometimes confused and disinclined for the midday meal. As breakfast is normally withheld on the morning of treatment, these patients often took little nourishment

* Made by Edison Swan Electric Co. and obtainable from Cox Cavendish Electrical Co.

DR. GRAHAM LESCHER: REFERENCES

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until tea-time. On being transferred to a smaller ward with better supervision and extra diet they improved and there was no further trouble. This is a point of some importance when large numbers of uncoöperative patients are being treated.

TABLE I—RESULTS IN 200 CASES

Diagnosis	All cases		Recovered		Imp.		Imp. in hospital		Not imp.	
	M	F	M	F	M	F	M	F	M	F
Schizophrenia	41	73	0	4	3	5	10	16	28	48
Affective psychoses—										
Mania ..	6	13	4	10	0	2	1	1	1	0
Depression ..	8	37	6	29	1	5	0	0	1	3
Mixed	2	9	1	3	1	2	0	0	0	4
Psychoneuroses	6	5	1	1	3	1	0	1	2	2
Total ..	200		59		23		29		89	

M and F = male and female. Imp. = improved.

RESULTS

The results of treating 63 males and 137 females are shown in table I. Cases have been classified in 5 diagnostic groups, but in the schizophrenic and affective illnesses only are numbers large enough to allow conclusions to be drawn. Under the heading "depression" are grouped melancholias and depressions, including involutional melancholia from whatever cause, and depressive phases of the manic-depressive psychosis; the schizophrenic group has not been subdivided.

The criteria of results are four: complete remission of symptoms with the return of full working capacity; partial recovery sufficiently great to enable the patient to remain outside hospital; maintained improvement social or ideational in patients still hospitalised; no improvement. Of the 200 patients, 20 men and 62 women were discharged from hospital; of these 12 men and 47 women made a complete recovery and none of these have since relapsed. This represents a discharge-rate of about 40% of all patients treated, irrespective of the nature or duration of the mental illness. It will be seen however that this figure is chiefly determined for the better by the proportion of affective psychotics treated and for the worse by the schizophrenics.

Schizophrenia.—Of 114 schizophrenics of both sexes only 12 left hospital, 4 women alone being considered to have recovered. The remaining 102 required institutional supervision, but in 26 of these some degree of sustained benefit was observed. In other words, treatment of 114 patients has been justified by some improvement in 38 cases, of which only 4 showed full remission.

TABLE II—RESULTS IN SCHIZOPHRENIA

Duration of illness	All cases		Recovered		Imp.		Imp. in hospital		Not imp.	
	M	F	M	F	M	F	M	F	M	F
Under 1 year	5	12	0	4	0	1	1	1	4	6
1–2 years ..	12	16	0	0	3	3	4	6	5	7
Over 2 years	24	45	0	0	0	1	5	9	19	35
Total ..	114		4		8		26		76	

It is debatable whether shock treatment of chronic schizophrenics is really worth while when allowance is made for spontaneous remissions. This becomes even more dubious when it can be reported that 2 schizophrenic women whose psychosis was quite unaffected by persistent shock therapy made spontaneous remissions several months later; one is now serving in the Forces and the other is almost fit to leave hospital. Moreover, 3 subjects, 2 women and 1 man who had been in hospital for upwards of six years failed to improve in any way with long courses of shock treatment, but have shown considerable and it seems increasing improvement after recent prefrontal leucotomy.

The duration of symptoms is usually taken into account in making a prognosis for shock therapy. Not all the recent cases of schizophrenia admitted to hospital were treated. A few were rejected on grounds of physical unfitness, permission for treatment was refused in 2, and as a small number were improving spontaneously it was not necessary to institute shock therapy. This explains the disproportionately small number of early cases in the series; the number treated who had been ill for less than a year is only 17. It is noteworthy that the only schizophrenics who recovered belonged to this group, and that the results of treatment are very much worse in illnesses of longer duration (table II). Nevertheless, since 13 out of 17 recent cases failed to improve at all it was not possible to make an optimistic prognosis in any clear-cut case of schizophrenia. No doubt some of the subjects classified in the mixed psychoses could be included with the schizophrenics, thereby influencing the results for the better.

On the whole, although this series contains a disproportionate number of chronic cases, it has been worth while treating schizophrenia in the hope of improvement without necessarily hoping for recovery.

Affective psychoses.—Of 64 patients with affective psychoses treated, 11 men and 46 women were discharged including 10 men and 39 women recovered; 2 men and 3 women failed to improve, 1 of each sex improved but still required hospital care because of the short periods of remission between maniacal phases. Most affective psychotics therefore recover or show much improvement with electrical shock treatment, so that cases which fail to respond are of particular interest. In this series, of the 3 women, 1 had a temporary remission and relapsed; she now presents the clinical picture of Simmonds's disease. The second is an agitated melancholic with additional obsessional features whose symptoms have not altered for more than 10 years. The third was a reactive depressive who failed to improve with shock treatment, but afterwards made a spontaneous recovery when certain domestic and situational difficulties had been settled. One man suffering from recurrent mania relapsed repeatedly so long as certain psychogenic causes in his home existed. He later made a spontaneous recovery. One man with reactive depression failed to improve and later died of pneumonia. In his case external psychogenic factors were operating throughout.

Mode of recovery.—Where the affective reaction seemed to be endogenous, improvement appeared within the first two weeks of treatment; this was especially noticeable in involutional cases in which recovery was smooth and uninterrupted. Where there were external factors of psychogenic importance temporary relapses were common. It seemed to be a necessary part of treatment to settle the psychogenic situation if a lasting cure was to be expected. Two cases of depression accentuated by the fear of air-raids made an apparent recovery only to relapse after a few days at home. Both eventually left hospital after further courses of shock treatment, apparently cured at a time when air-raids were less to be expected. One woman whose husband deserted her failed to maintain her improvement until a settlement had been arranged between him and her family. Other cases could be cited in which disappearance of symptoms after a short course of shock treatment was not enduring so long as provoking factors remained outstanding. This appears to be of some importance in making a prognosis. In all psychoses the outlook is better where there is a strong affective element, for it is on affective disturbances that convulsive therapy seems to exercise the greatest influence. This was demonstrated in all the cases of schizophrenic and mixed psychoses that showed improvement.

SUMMARY AND CONCLUSIONS

Electrically induced convulsion therapy is a safe and convenient method of physical treatment in mental disorders. It is highly satisfactory in affective reactions and especially in involutional melancholia, but it cannot be regarded as a specific, and to be successful should be accompanied by psychotherapy on general lines. Its value in chronic schizophrenic illnesses is towards promoting social improvement rather than cure; on recent

cases its effect may be much more favourable. No doubt, as others have found, really early treatment brings about a fair percentage of recovery.

There were no immediate fatalities in more than 200 cases of mental disorders treated by electrical convulsion therapy, but unrecognised latent tuberculosis may have been reactivated in 3. Three fractures were seen: of the humerus, the neck of the femur and of the dorsal vertebræ. The only schizophrenics that recovered had been ill for less than a year. Spontaneous remissions were observed in 2 schizophrenics after unsuccessful shock treatment, and prefrontal leucotomy was responsible for improvement in 3 other shock treatment failures.

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MEASURING CEREBROSPINAL FLUID PRESSURE

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THE Dattner lumbar-puncture has been used mainly in venereal diseases clinics. It has not been adopted by neurologists and physicians because the measurement of the spinal-fluid pressure is said to take fifteen minutes (Erskine and Johnson 1938).

The needle is based on the trocar and cannula principle, but the cannula is itself a fine (size 18) needle with a stylet within it. This fine needle of shaft length 10·5 cm. fits within a wider bore needle of shaft length 7 cm. A screw on the outer needle can be tightened to hold the inner one in place. In use the inner needle is arranged so that its point is level with that of the outer and the screw tightened. The whole needle is then introduced as far as the dura. The screw is loosened, the fine needle pushed into the theca and the screw tightened. The hole made in the dura is small. This prevents leakage of CSF, the probable cause of lumbar-puncture headaches (Ingvar 1923, Nelson 1930). This would agree with the findings of many VD clinics both here and on the continent that punctures can be done by this method on outpatients with fewer subsequent headaches than when Greenfield's, Pitkin's or Harris's needles are used on patients kept in bed for 24 hours afterwards (Erskine and Johnson 1938). To measure the pressure we have adopted the following procedure.

A clip is placed on the rubber tubing connecting the manometer to the needle. Sterile saline is introduced by means of a syringe and needle into the manometer bulb. The clip is loosened and saline allowed to run out until there is a column of fluid in the manometer equal to the expected CSF pressure; we usually select the 100 mm. mark. The puncture is then made. When the fine needle is within the theca fluid is aspirated just to the end of the needle. The manometer is then connected and the clip loosened. A continuous fluid system is thus formed from within the dura to the manometer. It is necessary to wait 1–2 minutes for the manometer level to become stationary. Queckenstedt's test can then be performed. Pressure should be applied first to the uppermost side (the side on which the patient is not lying), for when there is no block this gives a smaller rise than the under side. Thus a wait for the first reading to return to its resting value is avoided, since we may expect pressure on the second side to give a reading above that on the first. The rise is slower than with a wider needle, but with unilateral pressure a rise of 15–30 mm. in half a minute has been found to indicate no block. Bilateral pressure afterwards can give a further 20–30 mm. rise. A fall of 10–20 mm. will occur within one minute of releasing the pressure.

In a series of diagnostic punctures on hospital inpatients we have confirmed the pressure reading, by removing the inner needle, pushing the outer needle through the theca and re-taking the pressure in the usual way. The reading has always corresponded within 5 mm.

When the fluid is greatly thickened with cells this method is not applicable. But we have used it successfully with protein values of 400 mg. per 100 c.cm., and with fluid which looked like pure blood. If the fluid is too thick the outer needle can be introduced into the theca without making another puncture.

The technique is no more difficult than with ordinary single needles. One rapidly learns the feel of the outer needle piercing the ligaments, and the slight resilient "ping" as the inner needle enters the dura.

Besides the advantage of being able to make a full CSF examination on an ambulant patient with less fear of complications, we believe that in cases where pressure is thought or known to be high this is the method of election. Pressure can be read with the removal of only 0·5 c.cm. of fluid, and the risk of subsequent leakage through the dural tear is reduced. The chief limitation to the routine use of the Dattner needle—that the pressure cannot be satisfactorily recorded—thus seems to be removed.

We are grateful to Lieut.-Colonel G. O. Chambers, commanding officer of this hospital, for permission to publish this note.

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AIR ENTRY THROUGH TRANSFUSION SETS

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RECENTLY several deaths from air embolism following transfusion have been recorded. I would like to point out the ease, under certain conditions, with which large quantities of air can be pumped into a vein through a transfusion apparatus working solely by gravity. I performed the following experiments:

An ordinary blood transfusion apparatus was set up with a bottle of plasma instead of blood, so that visual observation might be more accurate. The apparatus consisted of the inverted plasma bottle, fitted with a rubber cork through which ran an inlet and an outlet tube. The outlet tube was connected by rubber tubing to a Laurie type of drip chamber, of which the side arm was attached to a short length of rubber tubing closed with a spring clip. From the drip chamber ran another length of rubber tubing to a metal connecting piece fixed to a standard intravenous needle. The needle was placed in a trough of water 6 cm. deep with a calibrated measuring cylinder inverted over it to measure the quantity of air that might emerge. The flow of plasma was controlled by means of a screw clamp on the rubber tubing above the drip chamber.

Expt. 1.—The flow through the drip chamber was adjusted to 2·5 drops per sec. and was left running for a few minutes. A fluid level was present in the drip chamber and no air came through the needle. Then the spring clip on the side tube was removed and, contrary to the usual teaching that the fluid in the chamber would rise and overflow through the side tube, the level immediately vanished and in a few moments air was coming through the needle at the rate of 23 c.cm. per min.

Expt. 2.—The flow through the drip chamber was adjusted to 0·67 drop per sec., with the spring clip closing the side arm. A leak in the rubber tubing was then simulated by plunging a no. 12 hypodermic needle into its lumen, 5 cm. below the fluid level in the drip chamber. Immediately air could be heard entering the tube, and in a few moments was being collected from the intravenous needle at the rate of 1·6 c.cm. per min. Throughout the fluid level in the drip chamber remained constant. The rate of flow was then increased to 1·3 drops per sec., and air was collected at 5·2 c.cm. per min. A further increase in the rate of flow to 2·8 drops per sec. resulted in air being collected at the rate of 10·3 c.cm. per min. No change was noticed in the fluid level in the chamber.

The venous pressure in the arm of a recumbent patient varies greatly with the exact position of the arm and the general condition of the patient. I have assumed it to

be equal to 6 cm. of water. Thus a column of fluid (of approximately the same specific gravity as water) connected to the vein and 6 cm. in height would be in equilibrium with the blood in the vein. If this column of fluid is lengthened to some 50 cm. and ends in a closed drip chamber, it is obvious that there is a negative pressure of 44 cm. of water in the drip chamber. Now if fluid is allowed to enter the drip chamber at a slow rate, it will also enter the vein at the same rate; but the negative pressure in the drip chamber will not be materially altered, since the maximum flow through the needle that is possible is much in excess of the amount entering the drip chamber. With the advent of a leak in the rubber tubing (and owing to the rubber shortage the risk of this increases daily) air is sucked into the tube. Fluid, however, is still flowing down the tube, and its surface tension holds it as a short column filling the lumen. Thus a column of air and fluid alternating will pass down the tube and through the needle.

A METHOD OF PREVENTION

The screw clamp, instead of being on the rubber tubing between the blood bottle and the drip chamber, should be clamped on the tubing only 2 or 3 cm. above the needle in the vein. In this position the rate of flow is as easily controlled as before, but in addition it will be found that there is now a positive pressure in the apparatus above the clamp and any leak occurring will allow fluid out and not air in.

LIVER ABSCESS FOLLOWING PERFORATED DUODENAL ULCER

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SOLITARY liver abscess as a sequel to a perforated duodenal ulcer is sufficiently rare to be worth recording. The following case presented great difficulty in diagnosis, the clinical picture being that of non-hæmolytic streptococcal septicæmia.

A man of 25 was first admitted to the Royal Hospital, Wolverhampton, on July 8, 1941, with a month's history of gastric dyspepsia, culminating in a sudden access of pain in the epigastrium on the day of admission. There was board-like abdominal rigidity with great tenderness, and the diagnosis of perforated duodenal ulcer was confirmed at operation, when the perforation was closed under general anæsthesia. After the operation he had a daily spike of temperature, ranging between 99° F. and 100° F. for the first week, which was attributed to a postoperative bronchitis. He was discharged to a convalescent home on July 27, and to his own home on Aug. 9. He was readmitted on Sept. 30 with a story of gnawing abdominal pain round the umbilicus, made worse by deep respiration; he was feverish, and had had shivering attacks for the past two weeks. He was very pale and toxic-looking with considerable mental hebetude; tongue furred, severe pyorrhœa, heart sounds very distant, slight tenderness in the right side of the abdomen; otherwise physical examination was negative. A provisional diagnosis of subphrenic abscess was not confirmed by radiograms of the abdomen, and the patient was too ill to be screened. Blood-count: red cells 3,200,000; Hb. 63%, white cells 12,300 (polymorphs 81%, lymphocytes 13%). Urine: a fair amount of albumin; scanty red cells; cultures grew no non-lactose-fermenting organisms; films of fæces showed pus and a little blood, cultures again grew no non-lactose-fermenting organisms. Widal test positive to typhoid H 1 in 500, paratyphoid A 1 in 25, paratyphoid B 1 in 50; negative to typhoid O; he had, however, had injections of TAB during the last war. Blood-culture yielded a profuse growth of non-hæmolytic streptococci.

He ran an intermittent temperature, which rose to 102° F. in the second week, when he began to have almost daily rigors. A course of sulphapyridine (2 g. followed by 1 g. 4-hourly for a week) was given, which brought down the temperature, but when the drug was discontinued it immediately rose to 101° F. On Oct. 17 his condition had greatly deteriorated, pulse had a very poor volume, blood-pressure 70/50 mm. Hg; heart sounds very faint, no bruits audible. Spleen was palpably enlarged, though soft, three finger-breadths below the costal margin. On Oct. 22, blood-count: 20,900 white cells (polymorphs 84%). Blood-culture again yielded non-hæmolytic streptococci. The agglutination to typhoid H had now risen to 1 in 1250. He continued to complain of intermittent acute pains in the right iliac fossa, while the temperature rose to 102° F. each evening, he looked jaundiced at times, becoming progressively anæmic (on Oct. 29 Hb. 38%, red cells 1,880,000) and towards the end drowsy. On Oct. 31 he was given 2 pints of blood and sulphathiazole was begun. In spite of these measures, however, he died on Nov. 4.

At autopsy, the liver was enlarged, but the external surface showed no abnormality. The right lobe contained a large abscess about 3 in. in diameter; cultures from this grew gram-positive cocci in chains. The spleen was enlarged and septic. Granular and contracted kidneys indicated a severe chronic nephritis.

I can find only 2 cases of this kind reported in the past 20 years and both were abroad.[1] The septicæmic state, wth enlargement of the spleen, subclinical jaundice, leucocytosis, drowsiness, and intermittent pyrexia with rigors, are typical of the liver-abscess syndrome whatever the organism.

I should like to thank Dr. J. H. Sheldon for permission to publish this case.

Medical Societies

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE

AT the meeting on July 23, a discussion on the

Treatment of Malaria

was opened by Sir RICKARD CHRISTOPHERS, FRS. Symptomatic treatment, intended to relieve the vomiting, nausea, high temperature and other distressing symptoms associated with malaria, is, he said, important, but we should not get far if, as physicians had once to do, we had to rely on such treatment alone. Nowadays our sheet anchor is the specific drug. Up to the last 10 years or so the only specific drug of any distinct potency was quinine. Cinchona no longer comes mainly, if at all, from the forests of Peru, but unfortunately its cultivation, especially that of the heavily quinine-bearing forms, has become more and more concentrated in Java, until for a long time that country has held a monopoly. With Java now closed to the allies we must look forward to the supply being seriously curtailed, and the production of substitutes must become a most urgent matter. Quinine is not the only alkaloid obtainable from cinchona; especially in the more robust and low-grade quinine-yielding species commonly grown in India it may form less than 10% of the total alkaloids. Cinchona contains four crystallisable alkaloids—quinine, quinidine, cinchonine and cinchonidine, as well as amorphous alkaloidal material termed quinoidine. Cinchonine and quinidine are about equally effective with quinine, while cinchonidine is also somewhat active. These other alkaloids occur in amounts collectively considerably greater than does quinine itself, and they have been in use, especially in India, extracted from the bark along with the quinine as cinchona febrifuge, or after the quinine has been removed as quinetum. Cinchona febrifuge contains about 7% quinine and 47% of other crystallisable alkaloids. A product of this type, totaquina, guaranteed to a standard content of not less than 70% crystallisable alkaloids, of which not less than a fifth must be quinine, was recommended by the League of Nations on the view that it would make an effective antimalarial remedy available to a greater proportion of the population.

Besides these naturally occurring alkaloids there are various derivatives of the quinine type, notably hydroquinine, considered by some authorities to be even more effective than quinine and to be free from some of its undesirable effects. However, it is doubtful whether total alkaloids or any quinine derivatives could meet the demand for efficient substitutes; for this purpose we must turn to recently developed synthetic antimalarials. About 1924–26 Schulemann, Schönhöfer, and Wingler, working in conjunction with Roehl, synthesised 'Plasmochin,' and this brilliant feat in chemotherapy enormously stimulated research. In 1932 Mietzsch and

1. Mazzine, O. F. *Arch. argent. Enferm. Apar. dig.* 1935, **10**, 579; Biesenberger, H. *Wien. klin. Wschr.* 1927, **39**, 1424.

Mauss, working with Kikuth, synthesised 'Atebrin,' probably the most powerful antimalarial at present known. A number of compounds of these two types were synthesised by Fourneau and are known as Fourneau compounds. Since then many more or less closely related compounds have been made in different countries. The main ones are mepacrine (*BP*), 'Quinacrine' and 'Acriquine,' which are probably identical with atebrin; pamaquin, 'Praequine,' Fourneau 710, 'Rhodoquine' and 'Plasmocide,' which are identical with plasmochin or 'Plasmoquine'; Fourneau 915 or 'Rhodoquine V'; and 'Certuna' and 'Cilional,' which have an effect similar to that of plasmochin with much less toxicity.

For practical purposes we have two well-established forms of compound in general use as synthetic antimalarials—viz. (to give them their English official names), mepacrine and pamaquin. Pamaquin has the remarkable property of acting on the sexual forms of the parasite. Attempts to control malaria in communities through this action have, however, not met with much success, though it may have a use in reducing the chances of the spread of infection from cases in hospital. It is more and more employed as a sort of adjuvant to quinine or mepacrine, especially in after-treatment and so-called prophylaxis, but is now rarely used in treating the acute disease, because it is rather toxic and not very effective against the asexual stages of the falciparum parasite. It is considered by many authorities to have a beneficial effect in reducing the liability to relapses especially when used in after-treatment or prophylaxis along with the more effective schizontocidal drugs quinine or mepacrine. For this purpose it is given in very small doses, usually not exceeding 0·02 gramme, and then for short periods or well spaced. It is also put up in combination with quinine in tablets. It is not thought desirable to administer it at the same time as mepacrine. Pamaquin cannot be considered as a satisfactory substitute for quinine in treatment of the acute disease or by itself in after-treatment or prophylaxis, but mepacrine is generally accepted as at least as effective as quinine in the acute disease in reducing liability to relapse and in so-called prophylaxis.

Since all our ideas regarding treatment have been largely built up on quinine, Sir Rickard Christophers recapitulated what has been learnt about the use of this drug. We are not now so insistent on timing our dosage to catch the sporulation forms, but try to ensure that there will always be a sufficiency of quinine in the blood through the period of treatment. Largely as a result of the splendid researches of Stephens and his collaborators at Liverpool during the last war we now know that the heroic doses once given are useless. We do not now give more than gr. 30 in a day—three doses of gr. 10—and many consider gr. 20 a day adequate in acute malaria. Again we know, largely from the Liverpool experiments, that it is no use trying to eradicate infection by unduly long administration; most authorities now prefer to space administration suitably, usually with an interval or change of treatment. About 7 days' treatment is commonly considered suitable to cover the period of the attack. For so-called prophylactic use there are the two common methods of gr. 5 (or 7) daily or gr. 15 on two successive days in the week; gr. 7 daily is probably the best dosage; gr. 10 daily is not suitable for long periods. A good deal has to be allowed for fatigue, sun, cold, &c. to which the treated person is exposed. In the main these results are applicable to mepacrine. With this drug we give not more than 0·3 gramme in the day in three doses of 0·1 g. The toxicity is not apparently great. There is a liability to some gastro-intestinal effects or abdominal pain, and, especially in native races, nervous or mental symptoms. Mepacrine has a definite cumulative effect, so that the total daily dosage is pretty well fixed, and the periods for which it is administered must be carefully watched. Usually in the acute attack it is given for not more than 7 days, and if necessary repeated again after an interval. In prophylaxis the dosage must be cautious—say 0·2 g. on two successive days in the week or even at longer intervals. Mepacrine is a powerful yellow dye and liable to give rise to yellow coloration of the skin, but this is in no way harmful; it is said that the sclerotics are not affected. It is supposed that mepacrine does not, like quinine, precipitate blackwater, but cases following mepacrine have been described. It is also said to be less liable to bring about abortion than quinine, but this is uncertain. There is one feature in which mepacrine has a clear advantage over quinine—in its suitability for intramuscular injection.

Treatment in the ordinary case of malaria is best carried out by oral administration, but if there are cerebral or other pernicious manifestations parenteral administration is not only a matter of necessity but of urgency. With quinine this must be by careful intravenous injection, either using a dilute solution or injecting the drug very slowly. Intramuscular use of quinine in such circumstances is unjustified as the necessary rapid absorption could not be expected. Intramuscular injection of quinine is not so much used in pernicious malaria as in chronic cases thought to be resistant. The use of intramuscular quinine for such a purpose is largely the perquisite of the doctor babu or low-class practitioner. In the opinion of many it amounts to malpractice. Probably the case is not malaria to start with. The results at best form a necrotic mass in the tissues and at the worst lead to tetanus or serious sloughing. Intramuscular injection of mepacrine, on the other hand, is accepted as a correct procedure, and it does not cause sloughing. Mepacrine methanosulphonate *BP* ('Atebrin Musonate,' 'Quinacrine Soluble'), a more soluble salt of the alkaloid, is put up in ampoules for injection. In mepacrine then we have a good substitute, and at present the only one, for quinine. That this is the last word in synthetic antimalarials is improbable. Thus certain arsenical compounds have been shown by Yorke to have a remarkable sterilising effect on certain forms of malaria. Sulphonamides have not so far given much indication of their usefulness. Glyn-Hughes, Laurie and Yorke have, in testing out compounds of the synthalin type, found that at least one of these, undecane-1 : 11-diamidine, is effective against malaria—an entirely new type of antimalarial compound.

LESSONS FROM THE LIVERPOOL SCHOOL

Prof. WARRINGTON YORKE said that two facts seem of overriding importance—that we have lost Java and with it over 90% of the world's supply of quinine; and that our troops are already operating in many malarious countries and many of our ships are calling at malarious ports. It seems obvious, therefore, that the demand for antimalarial drugs will increase enormously. This serious situation demands immediate action in the manufacture of an adequate quantity of the only efficient synthetic substitute for quinine, namely, mepacrine, and in the conservation of existing stocks of quinine. The only way in which we can materially conserve quinine is by using it as economically and efficiently as possible in the treatment of malaria. It is a remarkable fact that there is no unanimity of opinion on how it can best be used. The extremely low toxicity of quinine has encouraged the use of unnecessarily large doses. In the researches at the Liverpool school in the last war, an attempt was made to decide on the smallest amount of quinine necessary to control the acute attack. Patients suffering from acute simple tertian malaria were treated with quinine in doses ranging from gr. 5 to gr. 120 on each of two consecutive days only. Even in the group treated with gr. 5 parasites disappeared from the peripheral blood and the temperature became normal in over 80% of cases, and this always happened when the doses were gr. 10 or more. Within a few weeks, however, most cases in all the groups had relapsed—even those given gr. 90–120, which is beyond the limit of toleration for most people. These results suggested that in the treatment of acute simple tertian malaria nothing was to be gained by giving more than gr. 20 or gr. 30 on a couple of days, and that it was impossible to produce a sterilisans magna by pushing the dosage to a degree which was definitely toxic. A series of cases of acute malignant tertian malaria were given a similar two-day treatment of gr. 30 of quinine and here again the temperature became normal and trophozoites disappeared from the blood in all of them. With the object of finding whether a definite cure can be obtained by a long course of large doses of quinine, cases of simple tertian malaria were given daily doses of up to gr. 45 by mouth for as long as eight weeks, and others were given the same doses on two consecutive days only for the same period.

Although the infections were usually controlled while the patients were taking these long courses, many relapsed within a few weeks of the end of treatment. The general conclusion was that as a suppressive treatment interrupted is preferable to continuous quinine treatment in simple tertian malaria.

On these observations the method of treatment which has been successfully followed in Liverpool for many years has been devised. It consists in controlling the acute attack by giving gr. 30 of quinine sulphate in solution daily by mouth for four consecutive days; the patient is then discharged and told to take gr. 20 every Saturday and Sunday for the next eight weeks, and if he relapses after that to continue the week-end treatment for a further period. The dosage is very possibly on the liberal side, but before the present shortage that did not matter. Now it is necessary to take every step possible to reduce consumption. Regarding the imperative necessity of controlling the acute attack, especially in an unacclimatised population, there can be no doubt, but the amount of quinine used for prophylactic or suppressive purposes is probably much greater than that used for acute attacks, and much of that is wasted. It might well be argued that better results would be obtained from simply treating acute attacks. Suppressive treatment is obviously necessary for troops campaigning in malarious countries and for seamen voyaging to malarious ports, but treatment of the acute attack is essential, and if there is any shortage of antimalarials it is the suppressive form of treatment which must be drastically reduced. We must also not waste the drug in the treatment of acute attacks. Thus the total dosage in a course suggested by the Army medical authorities is gr. 400; if this is designed simply to treat the acute attack probably at least three-quarters of the quinine is wasted, and if it is intended to sterilise the infection it will fail; much quinine could be saved if it were abandoned. Profesor Yorke expressed surprise at Sir Rickard Christophers's denunciation of the intramuscular use of quinine. He agreed that the repeated administration of intramuscular injections in chronic malaria is simply a money-making device, but did not agree that the method is unjustified in serious cases with pernicious manifestations because the necessary rapid absorption could not be expected. He has found one or two intramuscular injections of quinine bihydrochloride invaluable in the treatment of really serious cases where the patient must absorb some of the drug quickly. Considerable quantities of injected quinine can be found in the muscles of experimental animals weeks after the injection, but sufficient is absorbed to produce the desired results. In Liverpool many hundreds of intramuscular injections have been given during the last 25 years; they have produced none of the suggested ill effects and have saved many lives.

Finally Professor Yorke referred to the so-called standard Army treatment of malaria, which runs as follows: days 1–2, quinine gr. 30 daily; days 3–7, mepacrine 0·3 g. daily; days 8–9, no treatment; days 10–14 pamaquin 0·03 g. daily. This bears no resemblance to Sinton's combined pamaquin-quinine treatment, and he asked whether there is any evidence that pamaquin given in this way does reduce the relapse-rate in either simple tertian or malignant tertian malaria, and if not what it does that the quinine or mepacrine alone would fail to do.

MALARIA IN A HYPERENDEMIC ZONE

Dr. WILLIAM HUGHES, of the Nigerian Medical Service, explained why the treatment of malaria in a hyperendemic zone presents problems which do not arise elsewhere. In endemic malaria the parasite is most often *Plasmodium vivax;* in hyperendemic malaria it is usually *P. falciparum.* In endemic malaria severe and fatal cases occur at all ages; in hyperendemic malaria nearly all the severe cases and all the mortality occur in childhood. In endemic zones the incidence and severity of the disease will be the same in the native population as among newcomers; in the hyperendemic zone while the native population flourishes the newcomers are rapidly killed off unless protected against infection or treated for the disease. In the endemic zone infection is comparatively scarce and immunity practically non-existent; in the hyperendemic zone infection is universal and intense during youth but declines towards old age as immunity is established. Hence an epidemic may arise in an endemic zone or among non-immunes when for any reason infection becomes more widespread and intense, whereas an epidemic cannot occur in the native population of a hyperendemic zone. On the whole, then, the native population in a hyperendemic area are well off compared with those in places where malaria is only endemic. Attempts at prevention of infection in a hyperendemic area by antilarval measures may do more harm than good, and even in the treatment of bouts of fever associated with infection we should try to interfere as little as possible with the development of immunity.

In such an area quinine should not be given in the vast majority of cases of malaria in adults, because natural recovery will take place without, it will probably interfere with the development of immunity, if quinine becomes scarce it should be reserved for the severe cases seen in children and immigrants, and finally because it confuses the diagnosis, so that, for example, a case of tuberculosis is treated as malaria in the early stages when it is most amenable to the correct treatment. According to Barber 48·6% of adults in Southern Nigeria show parasites in their blood, so that the usual diagnostic criteria—parasites and fever—do not hold in the hyperendemic zone. The indications for treatment in native children are difficult to define. They are in the process of gaining immunity—between the ages of 1 and 4 years the parasite rate is over 90%—and to treat infection per se will check this process. There are, of course, cases where urgent treatment is required. Fortunately the total amount of quinine needed to cure the fever is very small. Most cases require injections of quinine, and gr. 5 can be given intramuscularly with safety at any age. The potential severity of the disease finds an adequate medium of expression in adult Europeans. Immunity could never be allowed to develop in them on account of the virulent course the disease takes in uninfected adults. Prevention of infection by antilarval measures is not practicable. The habit of taking gr. 5 or so of quinine daily has stood the test of time, but has many drawbacks. The dose for each individual has to be adjusted, often by trial and error. It does not prevent infection and is inadequate once fever occurs. It so reduces the parasite content of the blood that it often confuses diagnosis, and is the indirect cause of low fever and so-called tropical neurasthenia. Possibly some cases of mental deterioration and alcoholism could be traced to it too.

The standard treatment for an attack of malaria in a European in Nigeria was gr. 20 a day while the fever lasted, gr. 15 daily for the next few days, gr. 10 daily for perhaps another week and then back to the routine gr. 5. There has recently been a reversion to heroic dosage. For the acute fever gr. 30 of quinine is given daily by mouth plus gr. 10 intravenously, together with 0·4 g. of mepacrine. The maintenance dose is gr. 15 of quinine and 0·1 g. of mepacrine daily. This heroic regime is unnecessary in most cases. There may be something to be said for the large maintenance dose in certain emergencies—for example, a civilian on a long trek or a soldier actually in the battle zone. Dr. Hughes prefers the usual textbook regime of gr. 30 daily for the acute stage and a maintenance dose of about gr. 5. Injections of quinine are often required. Fatal accidents have occurred with intravenous injections, due to giving quinine too rapidly in a concentrated solution. Intramuscular injection is safe and painless if the syringe is boiled immediately before use and the injection is given very slowly—2 minutes is not too long to take. Fever should be treated promptly. The advice to allow the fever to subside before giving quinine has led to fatalities on board ship. If quinine is not given quickly incessant vomiting and coma may develop. Headache is a common symptom when there is high fever and some residual headache may remain for anything up to three months in cerebral cases. It should be prevented by prompt treatment with quinine and aspirin. The patient can be instructed to take up to gr. 60 of aspirin a day if necessary. Purgatives are not necessary in the acute stage, and they cause abdominal distension by hurrying on the undigested food to ferment in the large bowel.

When a European leaves the hyperendemic zone the general rule has been to recommend gr. 5 of quinine daily for 2 months, but there have been many failures and some cases of blackwater fever with this regime. Dr. Hughes now recommends a course of mepacrine and quinine beginning ten days after leaving the coast. The course consists of 0·2 g. of mepacrine and two gr. 5 tablets of quinine daily for seven days. The results in fifteen cases have been successful. Whether strangers who visit the coast should take quinine depends on the length of stay, the localities they visit and the season of the year. If the probabilities are in favour of infection Dr. Hughes advises prophylactic quinine and after-treatment. In the treatment of blackwater fever alkali therapy is a sine qua non whether blood is transfused or not. The urine should be rendered alkaline within twenty-four hours. Low fever requires careful diagnosis. There are genuine cases which run a temperature of 99°–100° F. for weeks at a time. The most frequent causes are malaria and pyelitis. If quinine is discontinued for 4 or 5 days repeated examination of the blood will usually settle the diagnosis. A bout of fever with rigors in such cases is not a bad thing. The minimum period of convalescence after an attack of malaria should be a week from the last rise in temperature. As regards troops in a hyperendemic zone, Wenyon in his survey of malaria in Macedonia during the last war emphasised the impossibility of preventing malaria by antilarval measures in the fighting zone, and the last war was mainly static while this one is mobile. Antilarval measures are therefore out of the question now. It might be urged that under camp conditions troops could be protected from infection, but actually such protection is almost impossible to achieve. In the remote event of it being successful it might promote a feeling of false security.

SOME CLINICAL EXPERIENCE

Sir PHILIP MANSON-BAHR said he had never departed in the main from the opinions he based on his initial investigations into the synthetic antimalarial drugs. He had been the first in this country to investigate the potentialities of plasmoquine and plasmoquine compound in 1926 and 1927, and later had done similar work on atebrin. There could be no doubt that by their aid the therapeutics of malaria had been greatly improved. At present the rôle of pamaquin was as an adjunct to quinine in the treatment of benign tertian malaria, and especially in the prevention of relapses which constituted such a feature of this infection in the prolonged quinine anti-relapse treatment of former days. It was now fairly certain that relapses could be prevented by courses of moderate quinine and pamaquin dosage. Mepacrine, on the other hand, was of little service in suppressing this infection, but was specific for the subtertian form, especially in combination with quinine in small doses (gr. 10 daily). He had advocated this method in the past ten years and had seen no reason to regret it, but he was not impressed with the benefits of parenteral injections of mepacrine (atebrin musonate). Occasionally intramuscular abscesses formed and might be large. As regards intravenous injection he had reason to believe that in cerebral malaria its action was too slow to be effective and he had seen cases so treated which showed no signs of improvement till intravenous quinine (gr. 10 of the dihydrochloride) had been substituted. In a recent case there appeared to be no reduction in the number of circulating parasites, or alteration of their morphology, after two intravenous injections of atebrin musonate. He had been impressed with the prophylactic value of mepacrine in preventing the development of subtertian malaria, and he had for years advised a five-day course of mepacrine to be taken by officials and others during the homeward voyage from West Africa. He had always regarded intramuscular quinine as a most valuable therapeutic measure in severe subtertian malaria. He had never had serious mishap and he was convinced that the evil reputation this method had sometimes acquired was due to the practice of giving repeated injections into the same area; whereas two or at the most three injections were ample under any circumstances.

Reviews of Books

Stitt's Tropical Diseases

(6th ed.) RICHARD P. STRONG, M.D. Sc.D. London: H. K. Lewis. 2 vols. Pp. 1747. £5 5s.

IT is now thirteen years since the fifth edition of this book appeared; the sixth edition has been rewritten and has swelled to two volumes. Dr. Strong's aims have been to summarise our knowledge of the clinical manifestations and treatment of tropical diseases and of important zoological aspects and laboratory measures relating to diagnosis, prevention and transmission. As a result the book now takes its place as an authoritative work on tropical diseases. The arrangement is on an ætiological basis; he deals in turn with the protozoal, the bacterial and the virus diseases; the disorders of nutrition; diseases which cannot be satisfactorily classified; and the fungous and helminthic diseases. He admits that he has only considered briefly the more important cosmopolitan diseases encountered in warm countries; and in any case a book on tropical diseases in the strict sense would consist of two chapters—one on tokelau and the other on pinta. However, to give 12 pages to trench fever (which is neither an important cosmopolitan disease nor particularly incident to the tropics) and only one page to smallpox, admitted to be "the greatest scourge of the natives of tropical countries," is disproportionate; and to devote two pages to a detailed account of the magnesium sulphate treatment of tetanus while dismissing the use of bromethal in half a line is to emphasise a method which should now be allowed to die a natural death.

The first two sections dealing with the protozoal and bacterial infections are the best in the book, and the chapters on malaria and blackwater fever are full and could hardly be bettered. Ascension and St. Helena should be added to the list of tropical islands which are free from malaria, and the use of people who have lived in malarial countries as blood donors should be called impermissible, not merely dangerous. Sternal puncture—a method of investigation which should entirely replace splenic and hepatic puncture—is rightly advocated in malaria and in the leishmaniases. More might have been said of the work of the last ten years on sylvatic or jungle yellow fever, and on the recent work on typhus in Malaya. The chapter on sprue is somewhat inadequate but the other recognised disorders of nutrition are well described. The criteria used nowadays in making a diagnosis of beriberi are not discussed—unfortunately, since the estimation of blood pyruvic acid is unquestionably of value. Particular attention has been paid to the zoological aspects of the helminthic diseases. Pinta, now known to be caused by a treponema, is classified today among the bacterial instead of the fungous diseases. The probable connexion between clonorchiasis and primary carcinoma of the liver, and the use of the gold salts in the treatment of clonorchiasis both deserve some mention. The excellent appendix on tropical hygiene gives advice on everything from mosquito-boots to the "disinsectisation" of aircraft. The objectivity and freedom from bias are very pleasing throughout: for example, the remark "it is well to remember that not all degenerative diseases of the nervous system are due to deficiency of vitamin B_1."

Aids to Osteology

(4th ed.) NILS L. ECKHOFF, M.S. Lond., F.R.C.S. London: Baillière, Tindall and Cox. Pp. 260. 6s.

THIS book made its first appearance some twenty years ago. The last edition, like many other books, suffered from enemy action, but the opportunity thus made was used to review the text and introduce more figures. As a result Mr. Eckhoff has written a fourth edition of high level—clear, accurate in detail, and illustrated with figures likely to be of service to the reader who has not the bones themselves under his eyes. Unfortunately the illustrations are only in the sections dealing with the trunk and limbs; simple line drawings would make the Chinese puzzle of the skull bones much more comprehensible.

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THE LANCET

LONDON: SATURDAY, AUGUST 8, 1942

DIPHTHERIA IN THE IMMUNISED

IN analysing the incidence of diphtheria among the inoculated in Liverpool since 1925, GLOVER and WRIGHT[1] have drawn attention to an odd gap in reported results of immunisation. Many figures for the response to the Schick test or the antitoxin content of the blood after immunisation have been published, but there have been few records of what really matters—the subsequent history of such children as regards diphtheria infection. In Liverpool no Schick tests or antitoxin estimations were done; this was a plain clinical tale, though it points more than one moral. From October, 1925, to the end of 1938, 54,985 persons had been inoculated with five varieties of prophylactic, one of them (MT) now long obsolete. Among this total 396 had, up to the end of 1939, contracted diphtheria and 11 of them had died; all the fatal cases were in children under school-leaving age and 6 of them had been inoculated with the admittedly unsatisfactory MT. In every case, fatal or not, the virulence of the infecting strain was established; with few exceptions these were gravis or intermedius strains, all the fatal cases being caused by one or other. There is clear evidence too of the greater preponderance of these more virulent strains among inoculated patients than in diphtheria cases in the city as a whole. Yet cases in the inoculated were mostly very mild. Even so, GLOVER and WRIGHT consider that they were too numerous. In part their number is ascribed to the weak prophylactic (MT) used in the early days. No Schick tests were done after immunisation, so it is not possible to say whether the infected child was a Schick immune; some children of course are refractory to immunisation.

So much for the debit side of the account; to the credit of immunisation there is the outstanding fact that whereas between 1933 and 1939 the case-rate among uninoculated children under the age of 10 years averaged 11·3 per 1000 per annum, among inoculated children it ranged from 1·5 to 3·0. The observation that in Liverpool the diphtheria rate over the age of 10 is much the same in the uninoculated and inoculated deserves further epidemiological study. Much remains to be done. Liverpool is heavily infected with highly virulent strains of the diphtheria bacillus and is inhabited by a population coldly indifferent to the offer of free immunisation. Up to the end of 1939 only 6% of the preschool children and only 31% of those between 5 and 9 years had been inoculated. Since at least 30% of preschool children must be immunised to affect incidence it can be no surprise that there has been no decline. Liverpool has always been in the forefront of advances in public health and it is unlikely that this state of affairs will continue indefinitely provided personal approach to parents can be contrived and local practitioners coöperate fully.

Meanwhile, figures such as those of GLOVER and WRIGHT far from lessening confidence in immunisation should enhance it. The prophylactic used, in Liverpool as elsewhere, is all-important, and it is satisfactory to know the care that is now taken by the Ministry of Health, as the licensing authority, to ensure that APT issued to local authorities for the use of practitioners is of high antigenic potency.[2] It is important, too, as BOUSFIELD[3] points out, that statistics published from various sources should be comparable. If this is to be achieved, technique and the collection and presentation of data must be uniform; BOUSFIELD sets out more than twenty possible sources of error which may account for the widely divergent results of immunisation campaigns.

1. *Lancet*, Aug. 1, p. 133.

SYME'S AMPUTATION

ALMOST exactly 100 years ago[4] a boy of 16 was admitted under JAMES SYME in Edinburgh for multiple sinuses of the foot involving the tarsal bones. Amputation was essential but since both calcaneus and astragalus were involved Chopart's amputation, devised 50 years previously, was impossible and an amputation below the knee was the only alternative. SYME[5] decided to amputate through the ankle-joint and thereupon fashioned a flap from the heel, dissected out the calcaneus, and with some straight bone-cutting pliers which had lately been designed by LISTON removed both malleoli to leave an end-bearing tibial stump. Although some sepsis followed and there was partial sloughing of both upper and lower flaps he records a satisfactory result. A few months later a "medical gentleman" aged 25 was sent to him suffering from caries of the ankle-joint; here SYME[6] added to his operation by sawing off a slice of the tibial mortice. The adherent skin due to disease may have been partly responsible, yet the novice will be comforted to know that SYME buttonholed his flap in dissecting out the calcaneus. However, he records that this opening gave efficient drainage.

For over three-quarters of a century Syme's was regarded as the most satisfactory of all lower-limb amputations, though there were some modifications. The classical skin flap was found to be too bulky and an elliptical type of skin incision came to be employed, taking just over a finger's breadth of the heel sole, and the tibia was sawn through half an inch proximal to the articular surface. ELMSLIE in this country is usually said to have devised this; the French[7] call it Guyon's method, but he also retained a slice of calcaneus in the heel flap. After the last war the Ministry of Pensions surgeons at Roehampton had special opportunities for observing the results of different amputations, and they came to the conclusion that end-bearing stumps were unsatisfactory. Three-quarters of 12,000 cases where the stump was end-bearing had to have re-amputations; 38 out of 54 Syme cases had to be re-amputated. In 1927 the end-bearing stump operation became obsolete in the ministry's hospitals and they decided that even the Syme had to go. It was their experience that the Syme stump soon developed callosities and that the operation was difficult to do well, so that when the flap settled it was often displaced backwards or to one side. Any attempt at refashioning the flaps invariably failed. But their greatest objection to the

2. *Brit. med. J.* June 13, 1942, p. 734.
3. Bousfield, G. *Publ. Hlth*, June, 1942, p. 165.
4. Sept. 8, 1842.
5. *Lond. Edinb. mon. J. med. Sci.* 1843, **111**, 93.
6. *Ibid*, p. 274.
7. Broca, B. A. and Ducroquet, C. The Artificial Limb, London. Translated and edited by R. C. Elmslie. 1918, p. 78.

Syme stump was that no artificial limb could be fitted to conceal the disablement—and they contend that the man who has had his leg off must be made to walk, act and look as if his limb was absolutely normal.[8] Few could argue with the ministry, for not many surgeons did enough amputations, and this teaching came to be accepted. Of late the Canadians, led by GALLIE[9] and LE MESURIER,[10] have asserted that the surgeons of the ministry have been too hard on end-bearing stumps, in particular Syme amputations. In Canada the government also had a follow-up after the last war and over 2000 amputations have since been under constant supervision. Out of 53 Syme amputations, including 1 double, 7 needed subsequent minor operations such as removal of a neuroma, but not a single one has had to be re-amputated since 1922. Of these cases 20 have had their amputations for over twenty years, but their stumps show no œdema or circulatory disturbances and they can "stand and walk all day, follow the plough and work in the factory." The Canadian artificial limb for a Syme amputation differs slightly from ours in that the stump end is completely enclosed; the stump sits in a metal cup and a blocked leather bucket extending up from it is so shaped that the upper part takes some tibial bearing.

The low opinion of Syme's amputation does seem to need revising. At present, as LE MESURIER points out, anyone doing a Syme amputation is liable to find it re-amputated by someone else. It would be a pity if the operation was no longer taught in medical schools. There can be no doubt that for the agricultural labourer, and wherever expert mechanical-limb centres are not available—a large part of the globe—the Syme amputation is the method of choice; to do a day's work a man need merely shove his stump into an easily made broad boot. A peripatetic correspondent[11] with the Chinese forces mentions this difficulty of obtaining artificial limbs and says that out there every effort is therefore made to avoid amputations. A Syme amputation is not something to be rushed in the heat of battle, for sepsis spells certain failure for the stump. Indeed in war, unless circumstances are particularly propitious, immediate amputations through any site of election are undesirable. Amputation by flaps at the site of injury is the wiser choice, and the final amputation is a plastic procedure to be settled later. HUGGINS,[12] after extensive experience of amputations in the last war, laid down that the optimal time for re-amputation is when all œdema in the skin and deeper structures has subsided—usually after about four months. LE MESURIER maintains that a Syme must not be done above an inflamed wound, since the lymphatics are infected and sepsis is inevitable; nor for an arteriosclerotic lesion or one following cold or immersion. Attention to the details of the operation is particularly important. To prevent the flap slipping to either side or backwards careful strapping is required; it is probably the only amputation where nerve shortening is desirable. Despite drainage a hæmatoma will sometimes form, and immediate postoperative pain in the stump is often a sign of it. PERKINS, in a lecture at the British Postgraduate School, advised that in all amputations if a hæmatoma is diagnosed you should "pocket your pride, take the patient to the theatre and evacuate the clot." A failed Syme is not a disaster, nor is it a reflection on the surgeon, who in modern war has to handle severely mutilated tissues. But a failed below-knee amputation is a tragedy for the patient, and a primary tibial amputation at the site of election, performed for a foot injury, carries a heavy responsibility. Even under the best conditions the below-knee amputation does not invariably stand up to full wear, and an increasing number—10% at present—have to be fitted with ischial-bearing corsets. The outstanding disadvantage of the Syme amputation is the ungainly artificial limb. But for a man handsome is as handsome does and most of the limb is concealed by his trousers. For the woman ungainliness is undoubtedly a strong argument for a tibial election-site amputation, though it is surely not beyond the ingenuity of the makers to fashion a more shapely limb for the modern type of Syme amputation.

8. Langdale-Kelham, R. D. At the British Orthopædic Association meeting in Liverpool, 1942.
9. Gallie, W. E. *Ann. Surg.* 1941, **113**, 925; *Surg. Gynec. Obstet.* 1942, **74**, 370.
10. Le Mesurier, A. B. At the British Orthopædic Association meeting.
11. *Lancet*, 1942, i, 664.
12. Huggins, G. M. Amputation Stumps, London, 1918, p. 11.

HOW BIG OUR SMALL NEEDS

APPRECIATION of size and weight is a question of comparison and familiarity. Housewives think in terms of pounds and ounces and have a good idea of the value of each in terms of foodstuffs. We all know how many pennies it takes to make a trouser pocket uncomfortably full and heavy, and how many gallons are required to top up the tanks of our cars—but change the units and we are lost. Many who took a car to the continent in the old days will recall their confusion when they first had to buy petrol in litres. There may be still worse difficulties if the mind is called on to appraise a greater range of size or weight or distance than is usual in everyday life—the National Debt would be a poser to most people who visualise it in terms of their own salary, and the difficulty of grasping astronomical magnitudes has become a popular gambit. Few of us have even tried to size up our vitamin and mineral requirements in terms of our daily food. Here things are further complicated by the multiplicity of units and methods of expression; there are parts per million, gammas per gramme, mg. per 100 g. and so on. Workers in these subjects, moreover, make a point of emphasising the minute quantities of the substances which they can handle and which may be necessary for life, so that many doctors have resigned themselves to feeling that appreciation of the size and weight of "traces" is beyond them. They have lost, in consequence, a great deal of the interest attached to the recent work on nutrition.

Most people find it a help to get the data with which they are confronted into concrete terms or at any rate familiar units. Sometimes it helps to think of things in terms of oneself. A man is about 1 part per 100,000 of a big football crowd, or 1 part per million of the weight of the *Queen Mary*. Others find that 1 part per million, or 1 gamma per gramme, can be made understandable by calling them 0·1 mg. per 100 c.cm. Others again employ some standard of comparison such as a red blood corpuscle with which they are familiar. A glass of water, for example, containing 6,000,000 red blood corpuscles may be regarded as

holding 1 part of hæmoglobin per million parts of water. We are said, nowadays, to require 60 mg. of ascorbic acid every day for optimum health. This is 10–20 times less than our calcium requirement and is only 20 parts per million of our total intake of food and water. Looked at in another way, however, this is really quite a large amount and it could be weighed with accuracy on any good chemical balance. We require only a fifth of this weight of iron or zinc and much less copper per day. An adult's requirement of vitamin D is said to be 100 to 200 international units per day. This sounds a lot, but 1 gramme of calciferol contains 40,000,000 IU of vitamin D, so that by weight our daily requirement is only $\frac{1}{2000}$ to $\frac{1}{4000}$ of a milligramme. Our iodine requirement is greater but is also of this order of magnitude. These are very small amounts. Our D requirement is only about 1/300,000th of our calcium requirement—quite a bit smaller, as anyone will realise who has looked round the crowd at Twickenham during the interval of the Calcutta Cup match, but large enough to exert a profound influence upon it. Yet if our daily dose of D were made up into pills the size and weight of a red blood corpuscle we should have to take 30,000 pills a day: 20 pills a minute all round the 24 hours.

These calculations may seem mere frivolities, and admittedly they are only a variation on the old adage about big fleas having lesser fleas, but it may comfort some to realise that these lesser fleas have concrete sizable proportions and we need not proceed ad infinitum to visualise them.

Annotations

PLASMA FILTRATION

AN essential step in the preparation of citrated plasma suitable for storage as a blood substitute is its clarification and sterilisation by filtration through asbestos pads. Unfortunately this presents considerable practical difficulties, since passage through the filter induces clotting. Bushby and Whitby [1] suggested by way of explanation that, in the presence of magnesium ions from the asbestos, thrombin is formed from prothrombin adsorbed on the pads, and this leads to clotting. They believe that washing the pads with dilute alkali at intervals during filtration removes adsorbed prothrombin before its conversion to thrombin, since clotting of the filtrate is reduced. It is not however abolished, and larger or smaller clots usually develop during storage in bottles of citrated plasma filtered in this way. In some cases it is then difficult to decide whether a given bottle is contaminated or sterile, and it is always necessary to include a filter in the equipment used for transfusion. Bushby and Whitby [2] have now shown that if citrated plasma is made decidedly alkaline before filtration the filtrate does not clot, and they conclude that thrombin is not formed under these conditions. The excess alkalinity of the filtrate can be neutralised with carbon dioxide under pressure, so that the final product has the almost neutral reaction of the blood. Clinical tests of citrated plasma filtered by this method have proved satisfactory, and there is no chemical evidence of damage to the plasma proteins by the somewhat drastic incidental alkalinisation. The new method is more rapid and less wasteful than the earlier method, but cannot of course compare in simplicity with the filtration of serum. It is the possibility of preventing the entire waste of time-expired citrated blood by recovering plasma for storage which justifies persistence in plasma filtration. Since, however, most of the bottles of citrated blood now collected contribute ultimately to blood-substitute stores, it might seem wiser to collect clotted blood and store serum, maintaining the banks of citrated blood at that level which the experience of the Transfusion Services has shown to be necessary. Not only would the difficulties of plasma filtration thus be avoided but the stored product would be cleaner, since it is said [3] that at least 5% of bottles of blood collected are contaminated and hence should be processed without delay.

1. Bushby, S. R. M. and Whitby, L. E. H. *J. R. Army med. Cps*, 1941, **76**, 4.
2. *Ibid*, 1942, **78**, 255.

FAMINE RELIEF

THE food blockade of the continent is a blunderbuss which by definition does execution at short range without exact aim. Designed to starve our enemies into submission it helps to starve our friends in enemy-occupied countries. The Famine Relief Committee, formed as a result of two conferences of church leaders called by Dr. G. K. A. Bell, Bishop of Chichester, in the spring, has collected evidence on food conditions in Europe.[4] Famine is acute in Greece, where 320,000 deaths—five times the normal death-rate—were registered from August, 1941, till the end of March, 1942. Before the war 40% of necessary foodstuffs were imported into Greece; in December the average daily consumption of bread had been reduced from the normal 27 oz. to 2½ oz. or less. In January 900 deaths a day from famine were reported; children are naturally most affected, and were unable to resist epidemic diphtheria which swept Athens and the Piræus. In Belgium cases of starvation œdema are appearing, and scurvy, rickets, anæmia, dermatosis and eye infections are becoming common. Of children attending school two-thirds get hardly any breakfast, and a third get an inadequate midday dinner. The teachers cannot hope to maintain scholastic standards because the children are too apathetic to attend. In unoccupied France conditions are comparable with those in Europe in 1918; the infant mortality-rate increased 45% between 1939 and 1940. In occupied France the official rations exist only on paper, and only in the rural districts is it possible to maintain a reasonable standard of living. Rations allowed to the Poles are on a starvation level and the Jews in Poland get less still. The committee, which is under the chairmanship of Dr. Bell, and has Miss Pye as its honorary secretary, includes representatives of every section of Christian and Jewish thought in Great Britain. They plan, in coöperation with existing organisations, to send food, vitamins and medical aid into occupied countries wherever control is possible. This is not a fantastic undertaking, for in January, 1941, Germany guaranteed that no deduction for the benefit of armies of occupation would be made from shipments destined for necessitous people in occupied territories, and this guarantee seems to have been fully observed. Thanks to negotiations carried through by the British Government 4000 tons of food a month is reaching Greece through Turkey. The American Friends Service Committee is giving supplementary school meals to 85,000 children in unoccupied France, and is also supplementing feeding in refuge camps. The Commission for Polish Relief has been able to carry out controlled relief, 50,000 children being fed for 18 months; the Polish foreign office is satisfied that none of this food was taken by the Germans. The new Famine Relief Committee is anxious to see an informed public opinion in this country which will be ready to face the difficulties of controlled relief. Several important bodies including the Church of Scotland General Assembly, the Baptist Union of Great Britain and Ireland, and the Cambridge United Council of Christian Witness, have already

3. Macfarlane, R. G., Macsween, J. C., Mainwaring, B. R. S. and Parish, H. J. *Brit. med. J.* 1942, **i**, 377.
4. Food Conditions in Europe. Compiled by [Miss] E. M. Pye. Pp. 12. Obtainable from the Secretary of the Committee, Drayton House, Gordon Street, London, W.C.1. 3*d*.

advocated such relief. The committee suggests that regular and adequate supplies for Greece must have first place. In order that our Government may have evidence of public feeling the committee advises those interested to form local groups of sympathisers, to get people whose names will carry weight to write letters to the local press, and to arrange deputations to members of Parliament. Mr. Dingle Foot's recent statement[5] in the House of Commons sets out the directions in which it has already been possible to mitigate the effects of blockade. At present no stocks of food may be collected in Britain for relief, but the committee has decided to open a fund to be used for help in the invaded countries as soon as permission is granted; if permission is withheld until the end of the war, it will be used then for immediate help and reconstruction.

Two instructive booklets written for the Royal Institute of International Affairs, one on postwar relief in general[6] and the other on medical relief,[7] urge the need for setting up international relief machinery now so that it can be put in motion directly the war ends. When the last war ended there was a year of chaos in which vast numbers of people died from malnutrition and preventable disease on the continent before effective relief measures could be applied. The machinery might be controlled by either the Office d'Hygiène Publique at Vichy or the Health Organisation of the League of Nation at Geneva. The former, unluckily, is now largely German-controlled and has no personnel for relief work. The Health Organisation has already done extensive relief work in many of the distressed countries and its experience and the nucleus of its medical staff which still remains could perhaps be used at once when the war ends. It may however be better to set up an entirely new organisation with a commissioner and an advisory committee including representatives of the public-health services of each country. Fortunately it is not difficult to foresee what forms of medical relief will be required and a start should be made now to work out the details, as well as to build up a store of food and medical supplies. The first step is to decide on a central administrative body which will ensure that this time the efforts of voluntary and official organisations are not squandered through lack of coördination. Dr. Mackenzie also demonstrated that it is not too soon to plan the outlines of a permanent international medical organisation, though the problems it will have to face can as yet be only dimly discerned.

ANISEIKONIA

PEOPLE who have a different refractive error in their two eyes see ocular images of unequal size. For instance, if one eye is myopic and the other hypermetropic, the image in the latter will be the larger of the two, for a convex lens magnifies and a concave lens minifies. Provided that the disparity is not too great, these people achieve stereoscopic vision, though perhaps with some symptoms of strain. In 1935 Professor Ames,[8] working on physiological optics at the Dartmouth Eye Institute, Hanover, New Hampshire, reported that there was often a disparity in size of the optical images even in isometropia. To this difference, which could not be accounted for by refractive error, the term aniseikonia was applied. The difference was usually only 0·25–0·5%, but in people complaining of asthenopia it might be 1·5–1·75%. To diagnose the condition he invented the tipping table and an instrument named the eikonometer, and he prescribed special lenses for the condition. No exact figures of cases are yet available, but it seems that a third of his cases are relieved of their symptoms while another third report partial relief. Field,[9] of the North Western University medical school, finds, as one might expect, that most of the patients referred to him for aniseikonia were in need of more adequate refraction and investigation of their muscle balance and convergence powers. Until more convincing evidence is forthcoming most ophthalmologists will agree with Field that aniseikonia is not a common cause of asthenopia. It must be remembered that there are always some patients who will be relieved by the psychological effect of a lengthy investigation with elaborate instruments and the subsequent prescription of an expensive pair of glasses.

STRUCTURE OF VACCINIA

SLOWLY some of the mysteries of the viruses are being unravelled while others tend to become more complicated. It becomes increasingly clear that their properties as viruses are so divergent that generalities must be avoided. They range in size from those of vaccinia, myxoma, canary pox, lymphogranuloma venereum and rabies, all between 125 and 175 mμ in their largest diameter, down to poliomyelitis (human and mouse) at about 12 mμ and foot-and-mouth disease at about 10 mμ. The viruses of lymphogranuloma venereum and a new mouse pneumonitis virus are susceptible to the action of the sulphonamides and thus so far different from all the rest. Vaccinia, one of the largest and most highly organised of the viruses, has been intensively studied by Hoagland and his colleagues.[10] They found that the elementary bodies of vaccinia are composed chiefly of protein, thymonucleic acid, lipid and carbohydrate in concentrations not much different from those found in bacterial cells. They have since found small amounts of biotin and riboflavin present. In purified suspensions they have also found a copper constituent in a concentration amounting to 0·05% of the dry weight of the virus; a 25-fold increase occurring during purification of the virus. In contrast to this Sprince and Schoenbach[11] have failed to demonstrate significant amounts of riboflavin, pantothenic acid and biotin in moderately concentrated solutions of purified tobacco mosaic virus which is only about 1/5 the diameter of that of vaccinia. The elementary bodies of vaccinia have also been shown to respond to osmotic influences and to be antigenically complex. The use of the electron microscope has given new opportunities for observing any structural differences that may help to explain their action and differentiate between the bacteria and viruses. Von Borries and the Ruskas[12] in their original experiment found the virus particles of vaccinia somewhat oval in shape and uniformally opaque. Green, Anderson and Smadel[13] have obtained the same picture with unwashed stored preparations of vaccinia but when these were rewashed immediately before use they presented a high degree of regularity of external outline and internal form. The particles are almost rectangular in shape, resembling a brick, and contain five areas of condensation, the central one being slightly larger than the remaining four. Heating for an hour at 56° C., dehydration in a vacuum over P_2O_5 and drying from the frozen state did not appear to alter the internal structure. The various stages of dissolution by alkali treatment, ranging from swelling, blurring of the edges and decreasing density of the substance to complete laking, could be clearly seen. After exposure to hyperimmune vaccinia rabbit serum, the rewashed

5. See *Lancet*, Aug. 1, p. 136.
6. Relief and Reconstruction in Europe; an Interim Report by a Chatham House Study Group. London: Royal Institute of International Affairs. Pp. 40. 1s. 6d.
7. Medical Relief in Europe: Questions for Immediate Study. By Melville D. Mackenzie, MD. Pp. 67. 2s.
8. Ames, A. jun. *Amer. J. Ophthal.* 1935, **18**, 1014.
9. Field, H. B. *J. Amer. med. Ass.* 1942, **119**, 132.
10. Hoagland, C. L., Smadel, J. E. and Rivers, T. M. *J. exp. Med.* 1940, **71**, 737; Hoagland, C. L., Lavin, G. I., Smadel, J. E. and Rivers, T. M. *Ibid*, 1940, **72**, 139; Hoagland, C. L., Ward, S. M., Smadel, J. E. and Rivers, T. M. *Proc. Soc. exp. Biol. N.Y.* 1940, **45**, 669; *J. exp. Med.* 1941, **74**, 69, 133.
11. Sprince, H. and Schoenbach, E. B. *Proc. Soc. exp. Biol. N.Y.* 1942, **49**, 415.
12. Von Borries, B., Ruska, E. and Ruska, H. *Klin. Wschr.* 1938, **17**, 921.
13. Green, R. H., Anderson, T. F. and Smadel, J. E. *J. exp. Med.* 1942, **75**, 651.

particles appeared more dense than usual, no internal structure being visible. This suggests that some of the antibody remained attached to the virus particles. A somewhat similar finding in the case of bacteria indicates that soon more light may be thrown on the reaction between viruses and their antisera. It was not possible to designate the limiting structure which separates the virus from the surrounding medium as a semipermeable membrane. Green and his co-workers only say that the surface of the bodies appeared to be different from the main internal constituents. Ruska does not think that the viruses of variola, rabbit myxoma and ectromelia possess a membrane similar to that of the bacteria. However it seems certain that vaccinia virus has a morphological structure which in many respects approaches that of bacteria and differs from that of the plant viruses. This technique may later reveal such interesting facts as a difference in structure between freshly isolated strains and those long passaged in mammals or attenuated by passage in the developing chick embryo.

GASTRIC ACTIVITY AND FAT DIGESTION

THE action of fats on gastric digestion is peculiar but is slowly being clarified. It is now established that ingestion of fat will inhibit both motor and secretory activity of the stomach—the latter including both enzymes and acid, and affecting both chemical, mechanical and "psychic" secretion. Ivy and others have shown that this inhibition is at least partly dependent on an inhibitory hormone known as enterogastrone, which, released from the duodenal mucosa when fats or fatty acids reach that area, is absorbed into the circulation and thence depresses gastric activity. Quite why such an inhibitory mechanism exists is not yet apparent, but some recent experimental work of Tidwell and Cameron [1] suggests that it varies with the chemical composition of the fat ingested. Working with cats and rats, these investigators found that the more unsaturated fats tended to remain longest in the stomach, while the more saturated ones tended to cause least gastric inhibition and to get further down the intestinal tract in a given time. For instance, while 43% of a dose of olive oil could be recovered from the cat's stomach at the end of three hours, only 25% of tripalmitin, but as much as 71% of linseed oil could be found there after the same period. Similarly, whereas after three hours much of the palmitin was found in the cæcum, none of the linseed oil had by that time reached so far. In observations on one infant given a barium meal containing various types of fat they again found that the gastric emptying time when olive oil was used was more than twice as long (5¼ hr.) as when a palmitin and stearin mixture was given (2 hr.). From these results Tidwell and Cameron suggest that gastric inhibition is probably induced by the actual absorption of some fat from the upper intestine rather than by any purely physical properties of the fat itself. Thus they conclude from their findings that fat structure, fat absorption, and gastric inhibition run remarkably parallel—with saturated fats the intestinal absorption is more rapid as the carbon chain is shortened, and the more readily fats can be split the greater their absorption rate. The mechanism would thus depend in their view on the intestinal enterogastrone being liberated into the blood-stream only on actual absorption of some fat from the duodenum and not merely on the entry into the duodenum of fat as such; thus the more rapidly some absorption can occur the more quickly and completely will gastric inhibition take place. The exact part which this mechanism plays in the processes of digestion, and its precise applications in clinical medicine are far from clear. Whether the inhibition is merely a safeguard against fats (and other foods) entering the intestine more rapidly than they can be absorbed, or whether it is bound up with the acid-alkaline reactions of stomach and duodenum is not known. Certainly gastric emptying time and secretion are delicately balanced and highly adjustable processes, and their relation to the varying types and quantities of foods eaten is one of the factors on which the whole mechanism of digestion—and indigestion—depends. More work on these lines should help in the treatment and prevention of both major and minor dyspepsias.

1. Tidwell, H. C. and Cameron, E. S. *Bull. Johns Hopk. Hosp.* 1942, **70**, 362.

INFANTILE RICKETS IN AUSTRALIA

DISQUIETING evidence of the occurrence of rickets in 47% of a group of full-term infants at some period in the first year of life is reported [1] by F. W. Clements from the Australian Institute of Anatomy, Canberra. It is disquietening that the prevalence of rickets should be so extensive in a land richly provided with sunshine and all the more so when it is appreciated that the source of the material for study was the infant welfare centres of the Canberra Mothercraft Society where the very poor are not found "and the percentage of under-privileged is small." During the past 2½ years nearly 500 infants have been seen and examined radiographically for rickets. Of these 150 have had radiograms taken regularly each month during the first year of life and of 134 full-term infants who had completed this examination 63 or 47% showed definite evidence of mild rickets during the first year of life. Eight premature infants in the series all showed rickets. A child was considered to have suffered from rickets if one radiogram was obtained showing definite rachitic changes. "Doubtful" appearances that became normal in the next radiogram were not included as positive. In 80% the onset of rickets occurred before the sixteenth week. Connecting the radiographic findings with certain clinical aspects of the subject Clements reaches certain tentative conclusions. For example, as regards bony deformities it is recorded that 3 to 4 months after the rickets had healed the bones appeared to be normal, but it is proposed to follow these infants for some years for the possible development of knock-knee, bowleg and certain changes in the shape of the chest wall. A similar follow-up study will be made as regards the state of teeth. When the rickets persisted for more than three months some of the classical clinical signs appeared, particularly epiphyseal enlargement and hyperplasia of the costochondral junctions. Growth was not essentially affected unless the rickets lasted for four or five months. The infants appeared heavier than they actually were and looked pale, although hæmoglobin determinations showed no anæmia. Craniotabes was not found in this series. Indeed Clements insists that the mild rickets he detected radiologically does not give rise to sufficient clinical signs to make diagnosis possible except by X rays until it has persisted for more than three months. An analysis of the factors responsible for this high prevalence of mild rickets suggests that the calcium intake of the mother coupled with adequate absorption of the calcium is the most important. Postnatal feeding of the infant (and even of the mother in breast-fed infants) is also important, and it is not enough that the infant shall obtain enough calcium. "It is imperative that there shall be enough vitamin D in the body of the infant to ensure the highly efficient absorption of the calcium from the alimentary tract." Clements doubts if enough vitamin D can be developed by regular exposure to the sun and to prevent rickets this substance must be taken by mouth. Clements makes certain important recommendations as a result of his studies. Every expectant mother must have adequate calcium in her diet—secured by at least 1 pint of milk daily or large doses of calcium lactate or gluconate (120 grains of calcium lactate are equivalent in calcium to

1. *Med. J. Australia*, 1942, i, 336.

1 pint of milk). Equally important is the absorption of this calcium and vitamin D must be given to the pregnant woman. For postnatal prevention every infant, including the breast-fed, must receive vitamin D by mouth as early as is practicable. It is doubtful whether enough cod-liver oil can be given to the very young infant without upsetting the digestion, and Clements therefore advises a vitamin-D concentrate in a dosage of about 400 international units per day.

CONTINUOUS SPINAL ANÆSTHESIA

ANY method of anæsthesia which depends on the single injection of the whole dose has disadvantages. People vary in their susceptibility to drugs and a dose just sufficient in one person to maintain the right level of anæsthesia for the required time may be excessive for another person. In order to overcome this obstacle W. T. Lemmon and G. W. Paschal [1] have devised a technique for carrying out what they call serial fractional controllable intermittent spinal anæsthesia; and in an account of a series of 1000 operations they make out a very good case for the procedure. Naturally, since the needle has to be left in position throughout the operation, a special needle and a special mattress with a gap in it are needed in order to avoid all possibility of breaking the needle. Stout small-bore tubing 30 in. long connects the needle with the syringe, which has a Luer-Lok plug to meet the stopcock on the tubing and prevent any escape of cerebrospinal fluid. The authors use procaine hydrochloride ('Novocain'), dissolving 500 mg. in 10 c.cm. of CSF, of which 2–3 c.cm. are introduced into the subarachnoid space when the stopcock is closed. During the induction period the patient is kept in 5° Trendelenburg position. If after 10 min. the degree of analgesia is not enough an additional injection of 1 c.cm. is made, and other supplementary injections are made whenever necessary in the course of an operation. Lemmon and Paschal find it takes about 90 sec. for the added dose to exert its full effect. In long procedures they give the supplementary doses at fairly regular intervals, usually every 30 or 40 min. As preoperative medication they always give phenobarbitone on the night before operation as well as 3 hours before it, and also an injection of morphine and scopolamine. If necessary they repeat the morphine injection in the course of the operation either intravenously or subcutaneously. The average length of operation in the recorded series was 50·4 min., but one gastrectomy took over 3½ hours. The average dose used was 220 mg., though with operations above the diaphragm the usual dose needed was much higher than this, being 445 mg. A 5% solution made by dissolving the procaine crystals in the cerebrospinal fluid was found to be the most satisfactory strength. There were no deaths attributable to the anæsthetic, but headache and pulmonary complications were about as common as they are after the usual spinal methods.

CHRONIC STREPTOCOCCAL ULCERATION

F. W. Taylor [2] has found the hæmolytic streptococcus as the infecting organism in a series of cases of chronic ulcer of the extremities, and believes that this is a type of ulceration too little recognised because it is unsought; it responds dramatically to sulphanilamide by mouth. The ulcer is a distinct entity, not associated as a rule with vascular impairment. Children and young adults are mostly affected, the initial lesion being a slight cutaneous trauma such as an insect bite, not specially painful. The ulcer is indolent with slight surrounding reaction. The fact that the lesion is so chronic and is unassociated with lymphangitis or œdema is likely to prevent the surgeon suspecting its hæmolytic streptococcal origin. The organism is obtained from the ulcer in pure culture, or may have a contaminant, such as *Staphylococcus albus*. The lesion is quite distinct from the burrowing ulcers described by F. L. Meleney. Its margins are reddened and may or may not be undermined, while the base is covered with pale granulation tissue which exudes a watery serum. Among 31 cases in Taylor's series all but 2 appeared on the lower extremity, but two children showed several ulcers over the dorsum of the hand and arm. The ulcers ranged in diameter from 1 cm. to 6 cm., had been present from two weeks to four years, and had been treated with a great assortment of external applications. Treatment with sulphanilamide was mostly carried out in outpatients. The dose given to adults was 1·3–6 g. by mouth daily. Doses of 4–4·5 g. daily were sufficient, but smaller doses were on the whole ineffective. Only 19 of the 31 cases received adequate doses; these ulcers all healed, whatever their previous duration, in an average of just under a fortnight, and they remained healed. Taylor is now experimenting with local application of sulphanilamide, which he thinks should give good results.

1. *Surg. Gynec. Obstet.* 1942, **74**, 948.
2. *J. Amer. med. Ass.* 1942, **118**, 1196.

EMOTIONAL LEUCOCYTOSIS

THAT infection is not the only cause of leucocytosis has often been noted [1]; one of the most curious of these non-infective leucocytoses is that associated with emotion. A high white-cell count is not an uncommon finding in mental patients and the reasons advanced have been fever, dehydration, or some obscure infection. Wittkower [2] showed that leucocytosis could be caused by suggesting various emotions to hypnotised patients; this and similar investigations did not support the infection theory. Milhorat, Small, and Diethelm [3] have now studied the problem in mental patients. They took special care to use accurate methods, to get as near basal conditions as possible for the "resting" counts, and to avoid well-known traps like diurnal variation. In their group of 200 patients, 34 had infectious diseases which were likely to affect the white-cell count and 15 of them had counts of over 10,000 per c.mm.; excluding these, 26·5% had white-cell counts over the 10,000 per c.mm. mark. These leucocytoses were not limited to any particular mental disease, but they were clearly related to the emotional state of the patients. The behaviours most often associated with leucocytosis were "panic reaction, depression with agitation, excitement with overactivity and anxiety, and excitement with overactivity and elation." Sadness without anxiety, and elation without anger, were not accompanied by leucocytosis. Counts up to 21,000 per c.mm. were registered, but the differential count did not vary. No evidence of dehydration with consequent blood concentration was detected. Further evidence was provided by giving the patients intravenous 'Sodium Amytal' in doses sufficiently large (0·3–0·5 g.) to produce definite symptoms like slurring of speech; these doses were followed by mitigation of the exaggerated emotional state, and there was a corresponding fall in the elevated leucocyte count. When the leucocyte count was not raised, sodium amytal did not affect it, though the emotional changes were induced just the same. Sodium amytal was also given in the same dose to a patient with non-emotional leucocytosis, and although the narcotic effects appeared as usual the white-cell count remained raised. Milhorat and his colleagues attribute this emotional leucocytosis to a redistribution of leucocytes from the reservoirs in collapsed capillaries of resting muscle, liver, lungs and spleen brought about by the circulatory changes which accompany emotional reactions; as adrenaline is known to produce leucocytosis they suggest that this hormone has a part in the reactions. In all this they are in line with and confirm previous views.

1. See *Lancet*, 1941, ii, 42.
2. Wittkower, E. *Klin. Wschr.* 1929, **8**, 1082.
3. Milhorat, A. T., Small, S. M. and Diethelm, O. *Arch. Neurol. Psychiat.* 1942, **47**, 779.

DIGESTIBILITY OF NATIONAL WHEATMEAL

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ACCORDING to a statement attributed to Drummond (1942) the Ministry of Food were largely influenced by considerations of digestibility in advocating the adoption of the national wheatmeal loaf. It is therefore important that reliable figures should be available as a basis for comparing the digestibility of national wheatmeal with that of straight-run white flour.

Krebs and Mellanby (1942) recorded experimental results which cast some doubt on the validity of the figures used by the Food (War) Committee of the Royal Society (1917) and by myself (1941) in calculating balance sheets of the gains and losses of nutrients resulting from the raising of the extraction level of wheat. Unfortunately Krebs and Mellanby's experiments are open to serious criticism in both design and execution. In the first experiment the national wheatmeal used contained only 0·45% of fibre, against the standard of 0·60–0·85% suggested by the Accessory Food Factors Committee (1941) and a mode figure of 0·85% on 303 samples examined by the Research Association of British Flour-Millers (1942). In view of the well-recognised relationship between fibre content and digestibility, the use of the low fibre sample by Krebs and Mellanby clearly makes their results inapplicable to ordinary national wheatmeal. Moreover, they state that the white flour and national wheatmeal were derived from different grists. This, too, obviously lessens the value of their work, since variations are known to be very wide in the quality of individual consignments of wheat.

This error was also made by Wood (1941), who compared a sample of white flour from one grist with samples of three higher extraction flours from another grist. As a result, the figures for the digestibility of the white flour sample failed to fall in line with those of the other three flours (see graphs). Krebs and Mellanby have failed to note this, and in consequence wrongly accuse me of misquoting Wood's figures.

In their second experiment Krebs and Mellanby did not in fact compare the national wheatmeal with white flour at all: an attempt was made to arrive at a digestibility figure by comparing the fæcal output of a "control" diet of meat, fish, margarine, bacon, cheese, milk, potatoes, and mixed vegetables, with that of a diet in which unlimited quantities of national wheatmeal bread replaced half the mixed food intake. In the control period the energy intake was 1850 calories per day, in the experimental period 3450 calories per day, while the protein content of the experimental period was over double that of the control period. Moreover the final calculated digestibility was not merely compared with that of a white flour derived from a different grist but with a figure arrived at by Macrae and his colleagues (1941) in an entirely different experiment of entirely different design. The results obtained by individual workers vary so widely that such a comparison is meaningless.

If, then, the results recorded by Krebs and Mellanby cannot be accepted, what basis of calculation should be used in comparing the digestibilities of national wheatmeal and white flour? A review of the relevant literature over the past 40 years indicates that a reasonably sound basis can be arrived at without further experimental work. The object of the present article is to summarise the results recorded over this extended period, and to attempt to establish acceptable figures.

PERCENTAGE DIGESTIBILITY

The experimental methods adopted in most of the earlier work were similar, consisting of the direct substitution of one type of bread for another in a diet of otherwise constant composition. The analytical methods used were essentially those still employed in such work: the Kjeldahl method for total nitrogen, and a bomb calorimeter or calculation from the total proximate constituents for total energy. The types of flours used by different workers varied widely, however. Wood (1911) used flours of 70%, 80%, 88% and 92% extraction, while Rubner (1918), whose experiments were specifically concerned with Germany's war-time bread supply, used flours of 70%, 80%, and 95% extraction. Hamill (1911) based his conclusions on a thorough review of earlier American work which dealt in the main with white flour, so-called entire wheat flour, and Graham (wholemeal) flour. "Entire wheat flour" appears from Hamill's description to be similar to the present-day national wheatmeal. The Royal Society Committee's Report (1919) was concerned with two levels of extraction—78% and 88%. The work of Macrae and his colleagues was also carried out with flour of two extraction levels—73% and 100%. It will be seen, therefore, that the collected results cover a wide range of extraction levels and refer to work carried out in widely different localities and at varying dates.

An examination of these collected results shows that, while the *absolute* levels of digestibility varied widely from one set of experiments to another, all workers have recorded a considerable fall in digestibility with increasing extraction. The extent of this fall is shown in the graphs, in which the collected results have been plotted on a composite diagram after conversion to a common basis. For this purpose the digestibility of 70% extraction flour has been arbitrarily taken as 100%, and the remaining values have been recalculated in proportion.[1] The two graphs show clearly that all the curves fall as the extraction level rises, though the rate of fall varies widely with individual workers, the variation being greatest for the protein values. From these collected results it is possible to arrive at representative mean percentage reductions per unit increase in extraction level. The figures work out at 5% reduction in protein digestibility and 4% reduction in energy digestibility for each 10% increase in extraction. If such figures are applied to the mean absolute values of digestibility of white (70% extraction) bread, the results noted in the table are obtained. These values may be compared with

MEAN VALUES OF DIGESTIBILITY

Extraction level %	Percentage digestibility: Protein	Calories
70	*88*	*94*
75	85·7	92·1
85	81·4	88·4
Difference	4·3	3·7

the American figures recorded by Hamill for white flour and for the same flour with finely ground bran added, a mixture which might reasonably be compared with national wheatmeal. Hamill's figures of percentage digestibility, which agree closely with the mean values, are as follows:

	Protein	Calories
White flour	90·9	92·1
" " plus bran	85·9	87·6
Difference	5·0	4·5

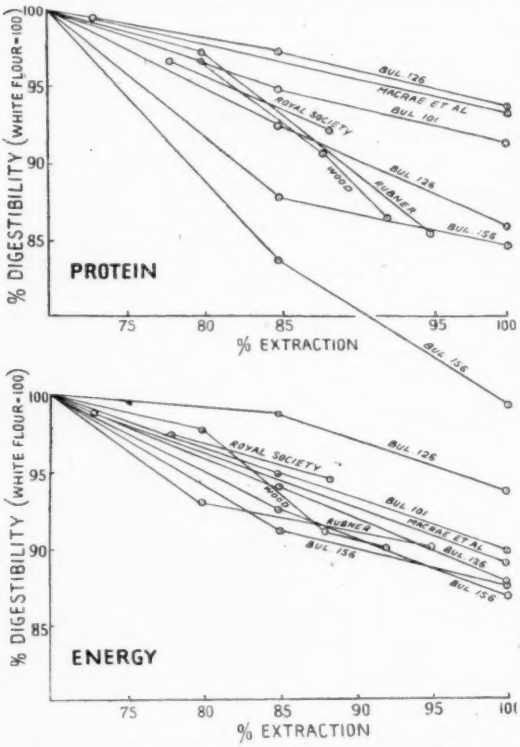
In general, the protein digestibility values recorded in the table show a significantly smaller difference than those which formed the basis of the Royal Society's original estimate and of my own calculations (89% and 81%) but a significantly larger difference than those recorded by Krebs and Mellanby (91% and 89%). The energy values closely approximate to our figures, which were 92% and 87% respectively, but again show a slightly larger difference than those of Krebs and Mellanby (97% and 94%).

PROTEIN AND ENERGY CONTENTS

In arriving at the total digestible nutrients contained in the two types of flour it is, however, at least equally important to take into account the relative contents of total protein and energy. As with the digestibility values, it is admittedly not easy to arrive at typical representative figures. As regards total protein, the mean values recorded in Hamill's review work out at 12·07% and 12·57% for white flour and wheatmeal respectively—a difference which agrees closely with that calculated from the analyses given by McCance and Widdowson (1940)—that is, 11·0% and 11·5%. At the

1. The figures given by the Royal Society relate to the digestibilities of the diet *as a whole*, and not to the bread alone. To obtain comparable figures for the various types of bread the results require recalculation. Wood's published figures for energy relate to percentage utilisation and not to actual digestibility: for the latter values recalculation is necessary. The figures used in the present paper are in both cases the recalculated values.

other extreme, the Rowett Institute tables (1938) give 12·6% and 11·7% for white flour and wholemeal which, if calculated for 75% and 85% extraction, would show a difference in the opposite direction of 0·3%. All these values are obtained by interpolation. A more satisfactory figure might be obtained from direct determinations on present-day samples of white flour and national wheatmeal. Typical analyses carried out by Gordon Hay (1941) give values of 12·0–12·1% for white flour and 12·38–12·44% for national wheatmeal, a difference of 0·35–0·38%. This difference is slightly higher than that



Graphs showing effect of extraction of wheat on the digestibility of the protein and energy of flour. Reference to Bulletins will be found in Hamill's review (1911) : for the remaining authorities see list of references at end of my paper.

recorded by Hamill for white flour with and without added bran (i.e., 0·29%). It thus appears that as I stated in my original paper, by adopting a difference of 0·5% both the Royal Society and I were unduly weighting the calculations against white flour, and that a figure of 0·35% would have been preferable.

A similar conflict of views is apparent in considering the energy contents of the two types of bread. Figures interpolated from the values given by McCance and Widdowson give 370 and 355 calories per 100 g. for white flour and wheatmeal respectively. The Rowett tables, on the other hand, show a negligible difference between the two flours, while the mean of Hamill's figures shows a slight balance in favour of wheatmeal. In these circumstances the adoption of the same value for both types of flour—364 calories per 100 g., the figure used by the Royal Society committee and myself—appears to be justified.

FINAL BALANCE SHEET

The problem which both the Royal Society committee and I attempted to solve was whether the raising of the extraction level by 10% (e.g., from 75% to 85%) would result in a net gain or loss of nutrients, taking into account not only the nutrients contained in the flour but also the value of the animal products produced from the available wheatfeed. The Royal Society committee assumed that this wheatfeed would be converted into pig-meat : for reasons stated in my earlier paper, I based my calculations on the assumption that it would be used for milk production. It appears from a recent statement made by the parliamentary secretary to the Ministry of Food (1942) that in the official view the loss of wheatfeed will result in a reduction in milk, eggs or meat. For the purpose of calculation, and particularly in view of the facts noted in a current article (Wright 1942), it will be simplest to adhere to my original basis of calculation. Bacharach (1941) has pointed out that a balance sheet can be drawn up in two ways : by assuming a constant weight of grain ; or by assuming a constant level of flour consumption. The former will give the *theoretical* gain or loss resulting from a change in the extraction level, the latter the *actual* loss of nutrients, taking into account the accompanying reduction in shipping tonnage.

Using the new digestibility figures and incidentally adopting a correction suggested by Lester Smith (1941), the first method indicates that the raising of the extraction level should theoretically result in the loss of about 1000 tons of protein but the gain of sufficient energy to supply about 40 calories per head per day—though at the cost of many million gallons of milk. The second method shows, however, that in actual practice the adoption of an 85% extraction level will result in a net annual loss of over 60,000 tons of protein as well as of over 1,600,000 million calories. Krebs and Mellanby state that my original arguments against the raising of the extraction of wheat to 85% are not substantiated by their new data. A re-examination of the balance sheet of nutrients in the light of the collected results reviewed in the present article does not support this rather sweeping assertion. If, as is now advocated by Sir Ernest Graham-Little (1942), the extraction rate were to be raised to 95–100% (that is, if the wholemeal loaf were to be compulsorily adopted) these already serious losses would be more than doubled.

SUMMARY

The results recorded by Krebs and Mellanby for the digestibility of national wheatmeal are open to criticism.

The collected results of earlier workers are reviewed, and the following mean values for protein digestibility adduced : white flour 86% ; national wheatmeal 81%. For energy digestibility mean values are : white flour 92% ; national wheatmeal 88%. For protein content : white flour 12·00% ; national wheatmeal 12·35%. For energy content : white flour and national wheatmeal, both 364 calories per 100 g.

Judging from these figures, the annual losses of nutrients resulting from the adoption of the national wheatmeal loaf amount to over 60,000 tons of protein and over 1,600,000 million calories ; adoption of the wholemeal loaf would more than double these losses.

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ROYAL COLLEGE OF OBSTETRICIANS AND GYNÆCOLOGISTS.—At a meeting of the council held on July 25, Sir William Fletcher Shaw was re-elected president. The following officers were also elected : vice-presidents, Prof. William Gough and Prof. C. G. Lowry ; hon. treasurer, Mr. J. P. Hedley ; hon. secretary, Mr. G. F. Gibberd ; hon. librarian, Wing-Commander Frederick Roques ; and hon. curator of museum, Mr. Aleck Bourne.

Dr. L. C. L. Averill, New Zealand, was admitted in absentia to the fellowship. The following were elected to the membership :

Herbert Agar, Muriel Boycott, J. W. D. Buttery, Marie H. Calverley, T. A. Gillie, I. M. Jackson, W. J. McCord, Mary K. Lawlor, H. M. Wolff, and J. F. B. Wyper.

In England Now

A Running Commentary by Peripatetic Correspondents

THE peripatetic who suggests "homo alternans" as a suitable generic name for mankind doesn't think a whole lot of us medical planners. Well, it is only fair to say that some of us don't think a whole lot of him. If he is not prepared to believe that, by taking thought, man can add a cubit to his material and moral stature, he will find a formidable array of hard fact and enlightened opinion ranged against him. The real subconscious (his word, not mine) argument against medical or any other kind of planning is that it is hard work; not only does it demand the acquisition of a great deal of information, some of which may be very distasteful to one's personal prejudices and cherished beliefs, but it also entails much critical and self-critical, constructive, and imaginative thinking. Why must all planning be probureaucratic and anti-individualistic? Does he really suppose that we are not considering the points of view of the warriors or that there are no planners among them? Does he assume that all these young men and women in the Services are so delighted with the world as it is or with medicine as she is practised that their one hope is to see her stay as she is for ever? And what about the 40 odd millions of patients, actual or potential, in these islands; are they all quite satisfied that they get the squarest possible deal when they are ill? All planners have always made, are making and will continue to make "enormous and manifold errors" and miscalculations; but the fact that we failed to create a new heaven and a new earth after the last war does not strike some of us as an adequate reason for not trying again. And despite the jeremiads, the cynicism (which Pasteur, I think, called sterile) and, worst of all, the resignation of the sub-group homo automaticus, try again we will.

* * *

Now that the crowds have melted, the President of the Board of Education is back in London, and they are pulling down the centenary bunting, we may creep out and examine with a little detachment that awesome, Jehovah-like figure with side-whiskers, deep-set eyes, and protruding lower lip, Thomas Arnold, "zealous, beneficent, firm." Mr. Butler said that had he been alive today he thought he would have approved of the educational reforms contemplated by Mr. Butler. This claiming as an ally somebody who is dead or not yet born like "the historian of the future" is all nonsense. In the unlikely event of the same dynamic, one might almost say anginal, Thomas Arnold reaching the age of 147 it may be safely said that he would not have approved, but fought like a tiger for these reforms 50 years ago. What he would be fighting for now is not vouchsafed to us; it would be 50 years ahead of our present ideas, for we have the myopia of mediocrity. When one remembers that "this champion alike of reverent faith and independent thought" very nearly had his career as a schoolmaster wrecked by scurrilous Tory attacks on his liberal opinions in social and theological matters I think it exceedingly doubtful whether he would have approved of Mr. Butler. or Mr. Butler of him. He was the antithesis of a yes-man, a big, capital No-man. In fact he would have made the last 50 years very uncomfortable for many of us, "sternly repressing the bad," entirely for our good. Like the mammoth, who may have taught man how to sprint, he was a great benefactor.

Which brings one to the obvious but little understood question of leadership in democracy. The real leaders are, of course, the Press, the Pulpit, and the Prevailing Wind—that is to say, original thinkers or strong characters or conglomerates. They put their views into circulation and after 1–50 years the people say, "That's rather a good idea, let's do it." Then they look round for some rather compliant individual and say, "Look here, you've got to go to Parliament and do this for us." That's why it's silly to think of political heads as leaders. It only rarely happens that strong characters can get the approval of Demos. Then it is as a rule on other than political grounds; hence the PM. In war-time matters are different, but one must not expect too much from the housemaid. Another schoolmaster who was a leader in the true sense, 50 years ahead of his time, who has done more perhaps for positive health than anyone in the last hundred years in this island except B-P, was Almond of Loretto. His ideals of hardiness and simple dress have been followed not only in this country but all over the Antipodes. Last week going through Pangbourne I was glad to see they have adopted the Loretto style at the Nautical College, now under an old Loretto boy. It is rather surprising that there haven't been more headmaster leaders, when one thinks of their opportunities of platform and constant stream of potential disciples. The reason, I think, is that most of them have been chosen for scholarship, a habit of word-thinking that cramps the vision, makes for stasis and orthodoxy, a form of specialisation from which few return, an irreversible addiction.

* * *

The medical transport officer put down his fourth glass of gin. "Thanks very much," he remarked, "I'll send those six cot cases and five walking cases over before the ship sails and I should keep an eye on three of them, they're a bit barmy." With that he departed and I rang up the sick bay to tell them what to expect, and that I would inspect them in the dogwatches. I sat down to lunch with the pleasant anticipation of getting my head down for the afternoon. At 14.15 I was rudely awakened by my sick-birth chief petty officer. He carried in his hand a well-thumbed copy of King's Rules and Instructions and with a sinking heart I saw his thumb on the part about the duties of the senior medical officer. With a further sinking I saw he had his leading sick-berth attendant with him and that he in his turn was loaded down with Admiralty Fleet Orders. The MTO's remarks, "three of them may be a bit barmy," suddenly came to my mind and we were three hours out of harbour. All too soon I was buried in orders. AFO 7932/22 was intensely depressing and seemed to indicate that ratings suffering from mental derangement should be under the constant eye of a medical officer. AFO 17532/26, however, was more cheerful and without doubt threw the whole onus on the captain of Marines. The little procession now headed by myself proceeded to the captain RM's cabin and to our delight we found he had his head down also. With considerable adroitness he parried every thrust until I pressed home with AFO 17532/26. He was a beaten man and the issue was no longer in doubt. Nine Royal Marines duly appeared in the sick bay and divided themselves into three watches. The isolation ward became our mental ward and for the rest of the voyage it rang with the delighted laughter of the escort and the dry remarks of our lunatics who were obviously highly enjoying themselves. The voyage continued peacefully, and our patients became the life and soul of the ship. During their spells of exercise on the fo'c'sle, they were more often than not the centre of a happy throng, and the captain's remark that "If those are lunatics the rest of us are stark raving mad" sounded rather true. This had been the opinion of the ward room for a good many months. The worse jobs the ship was given the happier the ship became, and for some time it had been noticed that officers visiting the ward-room viewed us with a slightly alarmed air.

It was difficult to explain the mental process of a young pilot who was returning on board in his aircraft from a duty trip to a station on the West Coast of Africa when he crashed on deck. He climbed out of the remains of his aircraft and with a hangdog air and his hands behind him approached the captain, who was fuming with rage at the end of the flight deck. Before the captain could let out his first bellow, the pilot produced a pineapple in each hand and said "I brought these for you, Sir." The war cry of the ship, which ward-room officers performed on suitable occasions, was a frequent cause of perturbation and the ammunition locker had often to be used for incarcerating young officers who became too disorientated. In such surroundings the lunatics became indistinguishable from ourselves and I still remember the efficient RAMC officer's expression when he came on board to collect them and was told that though they were labelled "Mentally Deranged" there was nothing the matter with them as far as we could see.

* * *

It was obvious when we arrived at the hotel why the proprietor had been so gushing over the telephone, promising us Room —, apparently the best in the house. The place was more than half empty. We had been

rather nervous when our inquiries were received so warmly. This was by no means the first hotel in the neighbourhood we had tried and they had all been full. And after all it was our first holiday since the outbreak of war and was only to last four days, including a Saturday and Sunday. It would be tragic if it was ruined by uncomfortable quarters. The plunge, however, was duly taken and not regretted. The only other male inhabitants, apart from myself, were the proprietor (a cast-off member of the aristocracy was our diagnosis), a waiter in his 30's (why wasn't he in the army ?) and a youth whose intelligence by no means matched his willingness. The visitors were the usual heterogeneous collection of females who seem to exist nowhere but in hotels, mostly rather antique, all very loquacious and none prepossessing.

Gastronomically we had little to complain of, but one piece of advice I would pass on to anyone who has not yet sampled hotel life in war-time: take your own marmalade. It was only provided on alternate mornings. Otherwise we were well cared for—eggs twice for breakfast, meat or fish for both lunch and dinner each day, though possibly the helpings were on the small side. Of beer and gin there seemed to be no scarcity; at least there was ample for my moderate purse. A large notice in the bar announced "No Doubles," but that did not prevent the platinum blonde who arrived for dinner one evening getting two "double gins" as an aperitif. Newspapers were unobtainable and as the only wireless set was invariably surrounded by a circle of chattering females at 9 o'clock we were deprived of the doubtful pleasure of hearing the news. For some odd reason there seemed to be no scarcity of Sunday newspapers; the waiter astonished us at Sunday breakfast by coming to ask which one we would prefer.

So passed the four days in arcadian calm—breakfast, a leisurely walk, lunch, siesta, tea, another stroll, drinks, dinner, bed. The only evidence of war was an occasional military lorry and a bar-load of Canadian soldiers in the evening. There was scarcely a car on the road, and even pedestrians were few and far between apart from "locals." And these Surrey lanes are lovely—a good second to the Cornish ones. The only depressing sight was the derelict appearance of so many of the lovely houses; not the stately mansions—these we avoided—but the smaller houses built and occupied by the successful professional, military or business man. They were still occupied but everywhere was evidence of neglect; paint was obviously considered a luxury, the flower gardens were overgrown, the hedgerows were uncut. Here was the impact of the war on this lovely countryside.

Yes, the hotel served our purpose well. It provided the panacea for all ills these days—a brief escape from the realities of the day. But (mention it not in Gath·) the main effect of my holiday was to make me thoroughly discontented for the next few weeks. The almost unbroken work habit of three years had been rudely shattered. When *would* the war end ?

* * *

A dozen times this year I have asked gardeners in action what they are thinking about, and I find their minds are projected three or four months ahead. That a man who is planting out lettuces should see and gloat over the prospect of their succulent maturity is not surprising, but that one working in the glory that is June should be filled with autumnal longings, or that he who might be enjoying the consummation of harvest should find the prospect of bleak December ploughland compellingly attractive, stirs thought. It is easy to see how this trick of prevision would quickly act selectively, benefiting and preserving him who stored, and staying the nomad. When some future Darwin comes to write the natural history of man, when the psychologists have waded out of the Freudian swamp, have climbed a little and distanced their horizon, then it may be found that this ability to see in pictures the scene some moons ahead, having divided birds into migratory and resident, having made hibernation in mammals possible, has played an important part in man's evolving. It is the essence of good husbandry and business, of strategy and the lust for planning; it is the cause of divine discontent with the present, and in the musically and aerially minded it has defined the life hereafter; but it has undoubtedly misled many into thinking they can spot the winner of the 2.30.

Letters to the Editor

WHAT IS GANGRENE?

SIR,—In a recent pathology examination the answers to a question on gangrene puzzled my coexaminer and me by stating, almost consistently, that gangrene is necrosis plus putrefaction. Each of us doubted this definition, having always held that bacteria play no constant part in the causation of the dry variety. However, we found that the answers reproduced what the students had been taught and that this teaching appears in many modern textbooks—e.g., Muir, Boyd and Karsner. Other books (e.g., MacCallum, Green and Aschoff) do not consider the presence of putrefactive bacteria essential to gangrene as a whole, though mentioning it, of course, in connexion with the moist variety. Kaufmann (1929) holds necrosis and gangrene to be interchangeable terms and writes "The entrance of organisms of decomposition produces softening, that is, moist gangrene."

A short search for evidence of putrefactive bacteria in dry gangrene was fruitless, and discussion in a group of four professors of pathology or bacteriology and a number of other experts betrayed a striking absence of corroboration. I came to the provisional conclusion that recent pathological writers have been over-anxious to find a scientific way of distinguishing gangrene from necrosis, and to this illicit and superfluous end have dragged in putrefaction. Superfluous because gangrene lays no claim to be a precise scientific term, being far more a clinical or at most a morbid-anatomical conception, and so it does not in the least compete with necrosis. Gangrene, in my view, is a gross manifestation of necrosis, with or without subsequent putrefaction. Surgical text-books (e.g., Illingworth) bear this out by defining gangrene simply as massive necrosis. On the other hand, there may be solid evidence that even in dry gangrene putrefactive bacteria are always present. Can any of your readers tell me where such evidence is to be found? If not, writers of pathological textbooks will perhaps make the necessary correction in their next editions.

Oxford. A. D. GARDNER.

CONSIDERATE TONSILLECTOMY

SIR,—It is encouraging to learn from Mr. Gerrie and Dr. Ross Mackenzie in your issue of June 27 that one more hospital has turned its back upon the barbarities of outpatient tonsillectomy in children, though one had supposed that a procedure so characteristic of the philosophy of blood and iron was already a thing of the past in this country.

It should, of course, be axiomatic that any form of surgical operation upon a child should be done without the child's knowledge, in so far as prevailing conditions permit, and that to this end basal narcosis should be as nearly as possible one hundred per cent. effective. For large numbers of children undergoing tonsillectomy in hospital the scheme described by Gerrie and Mackenzie is admirable, and I endorse their opinion that pentobarbital ('Nembutal') by the mouth is the best drug available for the basal narcosis. In the absence of the elixir, the powdered drug—not, of course, the capsule—is always taken without difficulty in honey, malt, or other such medium. By contrast, anybody who has often attempted it must know that rectal administrations of paraldehyde or bromethol frequently cause more psychic trauma—or, in plain language, no end of a rumpus—in a nervous child than does the clever administration of an anæsthetic.

The secrets of success with oral pentobarbital are organisation and taking trouble, and in this connexion I would add the following points to the Aberdeen scheme.

1. In non-hospital practice, either in a private hospital wing or in the child's own home—the latter in my experience the best place for tonsillectomy—much is to be gained by operating in the evening. The child goes to bed at the usual time, and with his invariable ritual except for the pleasant surprise of a teaspoonful of honey or what-not. He goes to sleep without question, and wakes in the morning with a sore throat, but otherwise oblivious that anything unusual has occurred in his familiar world. To expect a boisterous child to settle down to sleep at 9 A.M., though perhaps inevitable in hospital practice, is to give the game away at the first move.

2. The induction with ethyl chloride is better carried out as the child lies asleep in bed, before any moving is done.

3. At the first sign of restlessness after the operation, and in my experience this is more common than is implied by Gerrie and Mackenzie, an opiate should be given; 'Nepenthe' in doses of 1 min. per year of age is very efficient given hypodermically. This ensures quiet sleep for some hours and does not interfere with coughing or swallowing.

By these various means a guarantee in every case can be given to an anxious mother—rightly and reasonably anxious too—that her child will not know that he has had an anæsthetic or a tonsillectomy. There is no added risk in the anæsthetic, provided that it is given carefully and with knowledge; but again, have we not now left behind us the days when "just a whiff of anything" was good enough for a child's tonsils?

A Military Hospital. DOUGLAS BELFRAGE.

USELESS AND DOUBTFUL DRUGS

SIR,—Dr. Keele honestly displays his bias when he describes himself as a pharmacologist concerned largely with teaching students. It must be as annoying to such scientists to find practising physicians successfully using drugs which they have proved useless as it was, for example, to find people persistently using butter instead of margarine before the discovery of vitamins. Dr. Keele seems to have forgotten that it is impossible to prove a negative, and because he cannot in the laboratory find sound reasons for the use of a drug that is no sound reason for the exclusion of that drug from use; it is merely a sound reason for further research, preferably in the field of clinical medicine as well as in the laboratory.

The rôle of the pharmacologist is to discover the modus operandi of drugs rather than to decry the use of those whose mode of action he cannot discover. It is emphatically not his function to ask doctors to disbelieve their own experience because he has not himself made similar observations. The history of ergot and Barcroft's researches on fœtal respiration are both examples which justified the practice of the general practitioner and proved the dicta of the pharmacologist faulty. The teaching aim of the latter should be to instruct his students in technique and knowledge, and above all to cultivate in them that critical observation which will enable them later on to use drugs, not because they are recommended in books but because they themselves have proved their worth in actual practice. When a method of research proves a placebo more powerful than drugs used with success by practitioners I think it is at least as reasonable to question the validity of the method as to accept its conclusions. Such researches are statistically interesting, but we do not yet know enough about any people or disease satisfactorily to apply statistical methods to them. I remember Sir Ronald Ross about 1913 glorying in a lecture that our knowledge of malaria had reached such a stage that we could now apply to it the methods of higher mathematics, but experience in the last war soon proved him wrong. Angina may be a striking event, but its ætiology is not perfectly known, and I have little doubt that if W. Evans's cases had all been under their own doctor's care they would have received individual treatment with better general results. Individuality in treatment is essential in medical practice, but it is necessarily ignored in medical textbooks which have to treat abstractions as if they were realities—i.e., discuss diseases instead of patients—and all too often hospital practice follows suit.

About 1915 I was as complete a therapeutic nihilist as anyone, but I have come to have a great respect for some of the older physicians like Yeo and Brunton who discoursed at length about prescriptions not only with an air of conviction but as the result of long experience and observation. The wise physician does not prescribe "a small number of drugs with clearly demonstrated actions," he studies his patient and knows that the balance of the prescription is of real importance, and not infrequently finds that an apparently small change in it produces greatly enhanced results. Clinically I am often surprised at the way in which patients detect quite small alterations in their medicines even though there has been no appreciable difference in taste, &c., and almost always their description of the changed effect is what one might expect. Can Dr. Keele explain from his laboratory why small doses of diamorphine, for example, make some people bad, and why even so innocuous a substance as peppermint will make some patients really ill? It is easy enough to call it idiosyncrasy or "psychological," but this is only ignorance under another name; and it is these psychological troubles which trouble many of our patients and which one psychological bottle of medicine will help to put right while another equally psychological will not.

The trouble with Dr. Keele's teaching is probably that it is not based on experience in actual practice, and this is largely true even of the hospital consultants. They are debarred from private practice and as a result never get the day-to-day, and sometimes hour-to-hour, experience of their patients which a doctor gets in general practice. Instead they surround themselves with the tremendously curative properties which—in our present civilisation—are attached to the ideas of specialist and hospital. They can put the patient to bed in standard conditions, where they do little but investigate him for a week or two, by which time he has adapted himself to these conditions, and, unless he is suffering from the textbook diseases which Dr. Keele wishes to treat with his few standard "drugs with clearly demonstrated actions," he is sent out as cured or as having nothing discoverable wrong with him, only to relapse when he returns to his old conditions. While an inpatient he may have been treated with a bottle containing some simple drug or placebo, and the budding medical student has been shown how little is the actual effect of such medication in producing the cure, which, such as it is, mainly results from the regimen to which he has been subjected. Thus we breed a race of students ignorant of their own ignorance, and anxious when they are qualified to carry on their work in conditions similar to those to which they are accustomed in clinics, and so escape the troubles which harry the general practitioner and make up much of the sickness in this country.

For in general practice our patients mostly cannot afford to stop work; they come to us not to be labelled but to be treated and if possible cured. Their deviation from normal may not be great, but it is irritating or worse and often elusive. In such conditions most of us do contrive, largely by our bottles of medicine, to give some relief and help the person back to health without the loss of time or the capital expenditure of consultant or hospital. Let the consultant criticise our methods by all means, but let him remember that the problems and circumstances of our treatment are those that he himself has never actually encountered. The pharmacologist is still further removed from general practice. Perhaps we might even help to solve some of his problems if he did not so airily dismiss ours and pretend to a knowledge which is obviously incomplete. Doctors do not necessarily become fools when they become GPs, and some of us like to think we are doing our work as intelligently as we should if we had specialised in pharmacology.

This is not intended to deprecate the labours of pharmacologists or consultants, for few can appreciate their help more than I do. It is merely to deplore that we work largely in different worlds.

Winsford, Cheshire. W. N. LEAK.

SIR,—There is something about drugs which leads to extremes in the attitude of those who have to deal with them. On the one hand are the manufacturers of proprietary medicines—"ethical" as well as "non-ethical"—who tend to use nothing but superlatives in describing their products. On the other are the critics, who launch out into sweeping generalisations against medicines, revealing a spirit no more scientific than the others. Dr. Keele's letter of July 25 is an example of the latter class. How far is it correct to say that there is no sound empirical evidence that many drugs have any therapeutic value? What is sound empirical evidence? Dr. Keele is apparently prepared to accept the evidence of one investigator, Dr. Alstead, as sufficient to establish the inefficiency of ipecacuanha, iodides and bismuth oxycarbonate, but rejects the experience of innumerable practitioners. The folly of decrying such experience without the most thorough examination is well illustrated by the case of ext. ergotæ liq. of the BP

1914. This preparation was ridiculed by pharmacologists as worthless in spite of the strongest clinical evidence, only eventually to be shown to contain an active principle which fully justified the claims made for it. Alstead has certainly demonstrated to his own satisfaction that ipecacuanha and iodides are of little use in the treatment of chronic bronchitis, but his work has not been generally accepted. Furthermore, it may be true that bismuth oxycarbonate does not possess the property commonly assigned to it, but the way to settle the issue both in this case and in the others Dr. Keele is concerned about is not to "wonder"—as he does—how many drugs would fail to stand up to adequately controlled therapeutic tests but for him and his fellow pharmacologists to make such tests. This applies in particular to the few examples he quotes from the NWF. If there is any doubt about the value of ammon. carb. to diminish the unpleasant taste of cascara why not try it out? Even if creosote is not excreted in the sputum after oral administration it may still have a therapeutic effect. Search of the literature may give information or investigations should be made. I am surprised to find that Dr. Keele could be in any doubt about the use of mist. strych. et ferri. It surely is a tonic. The codeine in tab. codeinæ co. has an analgesic effect: to what extent it is responsible for the total analgesic effect is a problem for pharmacologists. I am wholeheartedly in agreement that the formulary should include only drugs that give convincing positive evidence of their worthiness, but any drug that gives therapeutic results should qualify for inclusion. I fail to see any distinction between pharmacological and psychological action; a psychological action clearly is a pharmacological action. It is the aim of such a formulary to include prescriptions that are needed, using the limited range of drugs available. It is up to the pharmacologists to teach clinical students what they believe to be rational therapy, and I trust they are not forced to discuss and recommend the use of drugs against their better judgment.

Pinner. H. W. TOMSKI.

THE MILK FACTOR IN CANCER

SIR,—The annotation on Bittner and his forerunners in your issue of July 25 prompts me to call attention to the fact that the milk factor in the transmission of disease to sucklings has exercised the minds of philosophers from very early times. The matter is discussed in Burton's "Anatomy of Melancholy," first published in 1621. The discussion naturally includes statements and records which might not bear critical investigation, but the following extracts are interesting and significant in view of the present-day scientific proof of a milk factor in the transmission of cancer in mice:

Aulus Gellius (a second-century Latin author) brings in Phavorinus, that eloquent philosopher, proving this at large, "that there is the same virtue and property in the milk as in the seed, and not in man alone, but in all other creatures." Giraldus (the literary name of the twelfth-century historian and ecclesiastic, Girald de Barri) came to the conclusion "that men and beasts participate of her nature and conditions by whose milk they are fed."

Portland Place, W.1. ALFRED WEBB-JOHNSON.

DIFFERENTIAL DIAGNOSIS OF DYSPEPSIA

SIR,—Sir Arthur Hurst and Major Venables misquote us in saying that we regard gastritis as the cause of severe symptoms. Certainly our conception of this condition appears to be different from theirs, but we went so far as to say that the symptoms were not so severe as those of peptic ulcer although, because of the lack of remissions and the intolerance of dietetic indiscretion, they tend to assume a greater significance. We maintain that symptoms in any organic disease can be materially affected by psychotherapy and suggestion, but Hurst's success in the symptomatic relief of his gastritis patients is no proof that the symptoms were those of an anxiety state.

With regard to other therapy, we have not been impressed by the results of simple diet and gastric lavage, having obtained maximal symptomatic and gastroscopic improvement only after adherence to the strictest dietetic regime with hourly feeding over a period of several weeks. We have been through our cases again and find that the duration of symptoms after the commencement of strict treatment is just twice as long for gastritis as for uncomplicated peptic ulcer. Cases of gastritis which were discharged before symptomatic relief was obtained are excluded from this estimate; if they could have been included, the comparison would have been more striking. At least half the soldiers with chronic bronchitis state that they have no cough, but on close questioning admit to a cough which they consider normal. Similarly many men with gastritis regard their "indigestion" as normal; the same is true even of some men with ulcer. In our opinion gastritis is paralleled rather by chronic bronchitis than by effort syndrone and, although a proportion of men with gastritis are symptomless because of their extraverted mentality, the symptoms complained of by the more introverted type are, nevertheless, primarily caused by their gastritis.

The radiological diagnosis of duodenitis, using Berg's technique, is founded on much more definite changes than is the case with gastritis. However, the crux of Sir Arthur Hurst's criticism is the absence of pathological confirmation; in fact many workers, including Kirklin, Nagel, Rivers, MacCarty and Wellbrook (to quote only references in English) have proved the diagnosis pathologically and have shown that superficial erosions and even massive hæmorrhages occur in duodenitis. In our series, for every five correct clinical diagnoses of duodenal ulcer, one was diagnosed as duodenitis: yet, of the duodenitis cases, for every one diagnosed wrongly as ulcer, four were clinically diagnosed correctly. We consider this degree of clinical accuracy significant.

A. MORTON GILL, R. ARDEN JONES.
An EMS Hospital. F. R. BERRIDGE.

DOSAGE OF LOCAL ANÆSTHETICS

SIR,—The most instructive article by Dr. Organe in your issue of July 11 prompts me to plead that drugs used for regional anæsthesia should be kept in powder form, contained in sterile ampoules. The powder (which has been accurately weighed by the maker) when dissolved in the appropriate amount of sterile normal saline (or CSF for subarachnoid block) gives a fresh, active anæsthetic solution of known strength and uniform reliability. Ready-made solutions tend to deteriorate on keeping, or may undergo a change in concentration, such as Dr. Organe describes in his first case where evaporation had increased the strength of the solution. The anæsthetist can never be sure how efficiently a ready-made solution has been prepared, and it is he who is responsible should any ill effects occur. I have never regretted adopting the method of preparing solutions which Labat many years ago advocated in his classic work.

Twickenham. NORMAN R. JAMES.

REACTIONS TO THE REPORT

SIR,—The demands on the personnel of our profession are more severe now than ever before and may well be harsher still. Many of us are hard put to it to keep things going while our colleagues are away. Under these circumstances, it is fantastic that members of the profession, some of whom were not specifically elected for the purpose, should be spending part of their time devising a scheme for a post-war world that no man can even visualise. We are an amazing people. Why all this urgency to produce a plan? Is it, as many think, because there is a certain group in medicine determined to introduce some form of state medical service at the earliest possible moment?

The majority scheme put forward would introduce so many changes in medical practice, as we know it at present, that it is frankly revolutionary. Revolutions of any kind are not popular in this country, especially when they are being pressed by the few upon the many. It is wrong to state, as a correspondent does in your issue of July 4, that "The majority of the public is only too aware of the many shortcomings of the medical services available to it." This is merely an assertion with nothing to support it. He accuses the profession of having "failed to give an intelligent lead to the public," and concludes by saying "This is our moment; let us have vision beyond tomorrow and build worthily for the future." That is a sad mixture of defeatism, emotionalism, and inaccuracy.

During the last few years it has been a favourite hobby of some, especially our left-wing intellectuals, to

decry our country, our mode of living and our institutions, and it was inevitable that sooner or later our profession would become the target. I submit we owe no apology to anyone, and we can look back on the past 20-odd years with the greatest satisfaction at the progress that has been made in giving better service to the public. By all means let the process of improvement go on, but what we need now, more than ever before, is progress based on stability. Let us build on what we already have. If radical changes in medicine are the necessity that some people think they are, then in all fairness let it be done at a time after the war when those now on service will have an opportunity of putting their views forward, and when the profession as a whole will have the help and advice of those who are now fully engaged in trying to preserve a future for all of us.

Cheam, Surrey. C. C. BROWN.

PERMISSIBLE ON OCCASION

SIR,—In his eloquent speech in the House of Commons on July 22, to which Medicus MP gave proper attention in your last issue, the Minister of Labour preached the public health gospel as a major help to efficiency and so to increased output. I sought, but missed the opportunity to point out that the demand for increased output may be carried to excess. Competition has its dangers. A stand must be made against the appeal, in the name of patriotism, for long hours, no holidays, Sunday labour. Like alcohol, these excesses may be permissible on occasion. But they are boomerangs; very soon they diminish efficiency and output. They are responsible for much reasonable absenteeism. There is no excuse for their continued practice. The Industrial Health Research Board has shown the limits and conditions of endurance; but its reports remain unread by those who are most concerned. Managements, in their own interest, should be required to know the Research Board's specific findings on stated experience.

House of Commons. FRANCIS FREMANTLE.

TREATMENT OF THE CRUSH SYNDROME

SIR,—Mr. Patey and Dr. Robertson's refutation of a toxæmia as the cause of the "crush syndrome" is a blow at a cherished conception; but I am with them in their heresy. Here are some of my reasons.

1. The occurrence of the syndrome when the main vessels of the limb, above or at the level of the injury, were destroyed at the time of injury, which puts out of court, entirely or mostly, the absorption of autolytic products.

2. The absence of the syndrome in cases of ischæmic myositis, due to bad splinting or tying a main vessel, leading to Volkmann's contracture, and its absence in street accidents before it became the practice to give massive transfusions.

3. The absence of a time relationship between the duration of burial and the development of grave renal failure in air-raid casualties. "The average period of burial or crushing has been about 8 hours, but we have recently seen a case in which the patient was trapped for only 45 minutes at most . . ." (Belsey, R. H. R. *Proc. R. Soc. Med.* 1941, **35**, 329). A man of 24 developed renal failure after having been "pinned for five minutes beneath an overturned Bren gun carrier" (Williamson, J. C. F. L. and Janes, J. M. *Ibid*, p. 336). The same happened to a man who was "extricated almost immediately" after a road accident (Graham, W. H. *Ibid*, p. 335). Of the cases published by the Medical Research Council subcommittee (*Brit. med. J.* 1941, i, 449) the average duration of burial of the 5 patients who recovered was nearly twice as long as that of the 5 who died. Even micro-organisms require a latent period, but reflex actions appear immediately. To such reflex action I assign the renal disability, evident on admission in all or in the great majority of air-raid casualties who subsequently develop grave renal failure. If a latent period for this does exist it is related to the time of admission and the giving of massive or even not massive transfusions. To suppose the renal disability starts from the time of release is to suppose that during the whole period of compression the blood-flow through the limb—the return of blood to the systemic circulation; absorption from the dying muscles—is stopped.

I cannot accept Patey and Robertson's alternative. They impute the crush syndrome to the "loss of blood constituents into the injured limb"; it thus becomes a deficiency disease. Truly, shock is a deficiency disease, but the deficiency consists not in a loss of particular chemical constituents from the blood: it is of a physical character. The occurrence of œdema in an injured limb, associated with the accession of blood to the skin by the application of heat in people who have been exposed on the battle-field or in bombed houses and have become dehydrated, explains the shock noted in many cases only after treatment—the application of heat—has begun. The limitation of œdema by bandaging, or the attractive other means advocated by Patey and Robertson as a means of preventing shock, is all to the good—it prevents the administration of a massive transfusion! But whether it prevents renal failure is another question.

In no. 7 of the MRC cases polyuria appeared with œdema, or close on its heels. A man of 34, buried for 22 hours, was admitted "cheerful," with "no shock," and shock did not develop. Oliguria was present from the start: on the second day, the output of urine was 300 c.cm.; on the third, 420 c.cm.; on the fourth, 420 c.cm. The note for the fourth day adds, "Both legs swelling rapidly and becoming œdematous"; next day the output of urine was 2190 c.cm. What other explanation of this can there be but that the vascular system, inundation of which had been attempted by pushing fluids but had been largely frustrated by vomiting, was decompressed by the rapid pouring out of fluid from the blood-stream into the legs, relieving turgescence of the kidneys? In the same way, in a case reported by Ruscoe Clarke (*Proc. R. Soc. Med.* 1941, **35**, 339), "Prior to operation"—an amputation—"marked oliguria accompanied a normal blood-pressure. . . . During and immediately after the operation, a marked drop in blood-pressure was accompanied by polyuria. . . ." Is it not curious that a marked fall of blood-pressure should be accompanied by polyuria? Patey and Robertson state that strong experimental support for their view has been furnished recently. I have not read the paper, but laboratory experiments cannot blot out the evidence which is afforded by clinical experience on man and appears in reports often in laconic remarks.

Essential conditions are sometimes missed, both in the laboratory and at the bedside, and the conclusions in consequence are misleading. Patey and Robertson's argument is an example. They say that positive intermittent pressure applied to an injured limb may prevent renal failure, and in their paper (*Lancet*, 1941, i, 780) they described a case (their case 3). But in their recent letter they omit to mention that the fluid intake in this case during the first 24 hours was only 1650 c.cm.; and on the second day only 1410 c.cm. The intake was deliberately restricted; it appeared to them "that large intravenous injections of plasma or crystalloids before or during the shock phase would tend primarily to increase the loss of blood constituents into the damaged limb, with subsequent promotion of traumatic œdema." That large intravenous injection of plasma, by inducing a turgescence, can have any pathological effect on the kidney, or that the fluid intake of 7440 c.cm. (3000 c.cm. by vein) during the first 24 hours in their case 1, in which compression treatment was not tried and the patient died from renal failure, caused or contributed to the renal failure was not considered. Nor did they discuss whether the restriction of fluid intake played any part in preventing renal failure in their case 3.

Two other points are passed by. One is whether heat was applied to the patients. In view of the case recorded by Richard Bright in 1827 (Osman, A. A. Original papers of Richard Bright on renal disease, London, 1937. Case 4), that of a man who, "being very hot by carrying a great weight," drank cold beer and lay on damp grass and developed renal failure and died, the state of the skin arterioles seems of consequence. The other point is the position of the patient's body. This is of the greatest importance; in my view the Trendelenburg position is the sheet anchor in the prevention and treatment of shock. When renal failure has developed, the best posture is the semi-sitting with the feet somewhat raised. Renal decapsulation is useless unless done early: in one of two cases published by Clifford White (*Proc. R. Soc. Med.* 1919, **12**, 28) the operation was followed by the passage of a large number of casts, absent before—the uriniferous tubules (the loops of Henle) could distend.

In a case I saw 10 years ago (Hayes, D. S. and Paramore, R. H. *Lancet*, 1935, ii, 554) anuria, which complicated an abdominal condition, was treated by two

injections of tropacocaine into the spinal canal; the idea was to relax the abdominal muscles and cause a fall of blood-pressure. As in Ruscoe Clarke's experience, the renal state was rapidly righted. The same result one may reasonably suppose would happen in cases of renal failure developing in air-raid casualties. The result in my case was magical, and when the man was seen last year he was still fit.

Rugby. R. H. PARAMORE.

Parliament

ON THE FLOOR OF THE HOUSE

MEDICUS M.P.

"FEW things have such an important bearing on morale as food," said Mr. Mabane, who has taken over the duties of Parliamentary secretary to the Ministry of Food from Major Lloyd George; and Mr. Hudson, as Minister of Agriculture, was able to give such a good report of production that our food is assured. The whole of Mr. Hudson's speech, which took about half an hour, was packed with facts and straight-punching statements. But he made a second speech of five words only when Mr. Owen Evans of Cardigan said that we were producing more than half the food-supplies of the country in the interjection "It is nearly two-thirds." With our present food production, our existing stores of imported foods, our reserves of meat on the hoof and the increase of agriculturally self-sufficient people to over two million we could live well, but with a reduced meat ration, if we imported practically nothing at all until next harvest. This change from an agriculture dependent on imported feeding-stuffs for its sheep, cattle and horses, and a human population dependent for a very large part of its bread, butter, eggs, meat and fruit on imports, to what is a self-sufficient agriculture is a revolution which deserves even higher praise than the House gave in the debate.

Well might Colonel Walter Elliot, himself minister of agriculture in the past, say that the Minister's statement pointed out "the shape of things to come." The Ministry of Food should continue after the war and food subsidy should be an integral part of our agricultural administration. Food subsidy at present, Mr. George Barnes told us, costs 125 millions a year. But private out-of-date marketing arrangements cost us 1500 millions a year, according to Mr. Evelyn Walkden, who has made himself an authority on this subject.* The prospect opens up of nationalised food marketing with continuance of food subsidies to agriculture still further reducing the cost of food. And in this war food is cheaper than in the war of 1914–18.

Mr. Hudson told us how these results had been obtained: on the one hand by a scientific direction of agriculture, on the other by a complete state control through the county agricultural committees of the use of land. This year there is to be in England and Wales an increase of tillage by 500,000 acres, mostly wheat, so that by next year we shall have 600,000 more acres under wheat. But with this there is a great increase in milk production and every farmer is asked to keep the maximum head of stock he can feed with his own resources. There is complete state control and the power of direction of farming to any extent required, but Mr. Hudson's policy is to work by getting the active coöperation and interest of the farmers, and he succeeds by making personal visits to all parts of the country, and by insisting on the recognition of the individuality of the farm, even of the field, and by decentralisation of administration. Perhaps the most striking aspect of Mr. Hudson's policy is his reliance upon and usage of scientific research. The Agricultural Research Council is the active instrument employed "to obtain the maximum possible knowledge and relate it to the needs of agriculture." The Agricultural Improvement Council, set up last year, has the duty to "get the results of research adopted and utilised more quickly in farming practice." In order to avoid overlapping of these two bodies the Minister has appointed a certain number of members of each body to be members of the other. And in addition there are frequent meetings of the two secretariats. The work of the Agricultural Improvement Council is decentralised, to the limit; practical demonstrations are arranged "not merely on two or three farms in a county belonging to a farm institute, but on many average farms, right down to farms in individual parishes." The results of the first year's experience of the working of this organisation of science and applied science is the assurance of the marriage of research and practice. "We are today," Mr. Hudson claimed, "making the maximum possible use of all the scientific agricultural knowledge that we can possibly lay our hands on." The Minister, however, is no mere utilitarian and he took pride not only in the increase of food production but in that mixed farming which, with its waving fields of crops of infinitely great variety of colour, had made the countryside so beautiful.

The debate was certainly on a high level but did not come up to the imaginative and farseeing level of the Minister's statement. Colonel Elliot protested against any return to the "wheat mining and wheat quarrying" that has gone on in Canada and the U.S.A. and other countries of the New World and which in the name of cheap food has destroyed English agriculture and produced the dust bowl of the Ohio valley. Flight Lieutenant Boothby tried to sell the oats of Aberdeen to the Ministry of Food—apparently quite willing buyers. Some members talked of the waste of potatoes—that is, the part of the insurance reserve not used this year—and Mr. Mabane was able to say that this amounted to only 2 days' supply for human consumption. A suggestion was also made about incorporating oats in bread. There are possibilities of this, but they are limited; and if we are to add rye and potatoes (we did use potatoes in the last war) bread will be a very motley compound.

With the minds of all members gravely concerned about the war situation in Russia and the possibility of relief to this threat to the Allied lines by opening a second front, this food debate was a relief. In one vital and fundamental matter—namely, food-supply—a second front based on these islands, and the production front in these islands, is secure.

FROM THE PRESS GALLERY

Tuberculosis in War-time

IN the House of Lords on July 28 Lord DAVIES drew attention to the failure of the Ministry of Health to deal with the staffing requirements of institutions for the treatment of tuberculosis. Since the war there had fortunately been no great increase in the number of cases but the number of deaths instead of continuing to fall had increased from 26,176 in 1938 to 28,669 in 1941. There were unfortunately many people awaiting institutional treatment—1507 in England, 400 in Wales and 652 in Scotland. This figure did not include ex-Service patients and in Wales there were a further 130 ex-Service men on the waiting-list. He appealed to the Ministry to increase the facilities for these people, to use empty beds in the emergency hospitals and, above all, to help institutions to keep open the beds they had. He thought the Government should withdraw Circular 2340, which, he alleged, aggravated the shortage of nurses. It gave women the choice of the type of institution in which they would serve and by refusing to allow girls of under 21 to volunteer for service in tuberculosis hospitals suggested that the risk of infection was greater there than in general hospitals. When men were being sent to fight Lord Davies thought women should be sent where their services were most needed and he asked that the Ministry of Labour should include nurses and hospital domestic staffs in the categories of essential or vital war work. He also urged that the proceedings of the Rushcliffe Committee should be expedited, and that the manufacture of instruments for mass radiology should be speeded-up.

Lord CORK and ORRERY suggested that it would ease the situation if the General Nursing Council would introduce three months in a sanatorium into the training of nurses and this would be an advantage educationally. Lord HUNTINGDON understood that 20% of the country's general practitioners had been called up by January, 1941, and since then another 1400 had been taken. Could army doctors not help overworked general practitioners? He pleaded for the compilation of a tuberculosis register by the General Nursing Council, similar to those for fever and mental nurses.

Lord DAWSON said that although we were rightly concerned with the increase of tuberculosis in this war, it was important to keep our sense of proportion. The total increase in mortality from tuberculosis since the war amounted to 13% in Great Britain. A more anxious feature was the selective character of the infection among different classes. As in the last war, there was a tendency for an increase of infection among young women, but in this war there had been a novelty in the extension of the infection among young children; particularly in the incidence of tuberculous meningitis, from which there had been increased mortality of 50%. But on the whole he believed tuberculosis was under control, and though 13% was a considerable figure there was no sign so far of the disease running away with us. Even in the peak year of 1938 there were nearly 250,000 people being looked after in tuberculosis dispensaries. Tuberculosis was a germ disease which did not come in waves. It was always with us, and its root was in almost every country. It was at once curable and at the same time very destructive. It could destroy life in a few weeks, but most cases were so mild that the patients were not even aware that they had been attacked. In a country like ours, where a large proportion of the cattle were tuberculous, it would be wise to pasteurise our milk. The medical profession had been pleading for years with successive Governments to make pasteurisation compulsory. But prewar Governments had been stiff-necked and pasteurisation was patchy—not so good in the country as in London and some of the larger centres. Lord Dawson suggested that the increase in tuberculosis in children might be partly accounted for by the fact that owing to evacuation so many had consumed raw instead of pasteurised milk. Lung tubercle was caused by contact with the expectoration of an established case; and under the overcrowded conditions of war the opportunities of contracting tubercle must be greater than in peace. The difficulty of diagnosis of patients with vague symptoms was a matter for watchfulness. Mass radiography was making progress, and we were not dependent solely on the United States. There were machines in this country which had been standardised according to an agreed pattern, and which would now be turned out in increasing numbers. In skilled hands 3000 examinations a week were possible. He thought we could do far better in this country by persuasion than by compulsion, that mass radiography would be received with increasing favour as people got to understand it. But it must grow into our system of medicine discreetly, and to dispatch machines all over the country without proper teams to work them would make a bad beginning. Lord Dawson was doubtful about the education of the public by cinema: it was difficult to give information about health without causing alarm. Workers might swing from indifference to over-anxiety, and he himself almost preferred indifference. The rehabilitation of the tuberculous patient had not been sufficiently provided for in the past but he believed that the Ministry proposed to consider seriously the maintenance and subsidising of tuberculous patients from the time they leave the sanatorium till they return to full employment. In England the care of the tuberculous was primarily the duty of the local authority, but Lord Dawson thought that the emergency medical service might appropriately provide on a larger scale for tuberculous people. If it were made clear that there was no more risk of a nurse catching disease in a sanatorium than in an ordinary hospital—in fact rather less, if anything—and if in some way the tuberculous patient could be made part of a nurse's duties—she might for example be seconded from medical or surgical wards to tuberculosis wards—he believed that the nursing difficulty could to a large extent be overcome. But he was sure that any attempt to compel nurses to take up any particular phase of nursing would end in failure.

Lord SNELL, replying, said that we must remember that the shortage of nurses and domestics is only one phase of the Government's problem to make the best use of woman-power. Though the position was unsatisfactory it is slightly better than a year ago. Over 90,000 nurses were now working in civilian hospitals—8000 more than a year ago. It was estimated that another 12,000 nurses were required. There were 2000 nurses employed at sanatoria and another 600 were required and a further 600 for tuberculosis beds in other hospitals. He admitted that the percentage deficiency was therefore higher in sanatoria than in general hospitals and that experience showed that tuberculosis nursing was not so attractive as other services. The Government was reluctant to adopt compulsion for nurses, but Lord Snell said that in the last resort they might have to consider a wider exercise of powers of direction. The decision not to allocate nursing auxiliaries under 21 years of age to sanatoria, even if they volunteered, had been taken by the Minister on medical advice that this age-group might be particularly liable to infection. A proposal had been put before the Standing Advisory Committee on Tuberculosis by one of its own members that the Ministry should be asked to withdraw the embargo. The committee felt unable to agree to this but had suggested young nurses might be allowed to serve in institutions dealing with non-pulmonary tuberculosis. This recommendation was adopted in Circular 2526. The Government had lately reconsidered the matter and they felt that perhaps in present circumstances nursing auxiliaries under 21 might be allowed to serve in sanatoria if they volunteered, provided that the fullest precautions were observed in looking after their health.

Summing up, he said we must not forget the improvement in the general health of the community which someone had impishly suggested might be due to the call-up of 10,000 doctors, but Lord Snell felt that we should defer criticism of the doctor until he had been provided with the social conditions to make his work effective. The Minister of Health shared in the anxiety felt at the new encroachment of tuberculosis and he would continue to take every means open to him to get staff deficiencies remedied and the needs of an essential service fully met.

QUESTION TIME

Quality of the National Loaf

Sir E. GRAHAM-LITTLE asked the Parliamentary Secretary to the Ministry of Food whether his attention had been drawn to the experiments conducted by three scientists of the Children's Nutrition Council of Cambridge, in which they examined 17 samples of national bread obtained from widely different sources, in 7 of which the Ministry's specification with regard to the maximum fibre content was not complied with.—Mr. W. MABANE replied: These experiments were made on flours milled before national flour became compulsory and confirm to a large extent the results of the larger survey carried out on similar flours by the Research Association of British Flour Millers on behalf of my department. The difficulties connected with the standardisation of so small a part of a miller's production were removed when national flour became compulsory and this report recognises the improved quality of national flour since its compulsory introduction.

In reply to a further question Mr. MABANE said that in the two weeks ending on July 11, the average production of wheat-germ by controlled millers was at the rate of 19 tons per week.

Sale of Tuberculin-tested Cows

Mr. DAVID ADAMS asked the Minister of Agriculture whether he was aware that it is common for cows which react to test for tuberculosis to be sent to market and sold as healthy cows, thereby spreading the disease; and whether prompt steps would be taken to prevent this practice.—Mr. R. S. HUDSON replied: The sale of cows reacting to the tuberculin test is not, on that account, restricted. In view of the very much larger number of untested cattle which, if tested, would react, no such restriction would serve any useful purposes.—Mr. ADAMS: Is the Minister aware that many cows seriously affected with tuberculosis are permitted to be put on the market and disposed as healthy cows? Is that satisfactory? Mr. HUDSON: That is merely repeating the question which I have answered.

Scientific Coöperation with Russia

Mr. R. K. LAW, in answer to a question, stated that some fifty inquiries from British men of science and scientific institutions have already been forwarded through the British Council to Soviet scientific institutions in the last eight months. Exchange of information has been encouraged by the formation by the council and Ministry of Information of a joint advisory committee of British men of science whose chairman is Sir John Russell of the Ministry, and vice-chairman and secretary officials of the council.

Notes and News

University of Oxford

In congregations held on July 18 and 25, the following degrees were conferred :

DM.—J. M. L. Burtenshaw.

MCh.—A. H. Hunt and R. H. Gardiner.

BM, BCh.—M. H. M. Gilbertson, J. F. D. Frazer, D. S. Parsons, J. L. Boldero, J. D. Little, R. F. B. Bennett, Q. J. G. Hobson, W. D. M. Paton, W. A. Briscoe, H. G. Farquhar, J. D. Green, J. Pinching, K. W. Lovel, S. L. H. Smith, * J. M. Jefferson, * H. J. C. J. L'Etang, R. H. Scott, R. Bryce-Smith, P. J. Crerar, D. M. Hamilton, R. Powell, D. A. McDonald, N. G. D. Campbell, R. H. Jackson, A. K. Tyler, A. M. M. Wilson, E. Shephard, W. B. Armstrong, E. L. H. Jones, G. A. Neligan, C. P. Silver, J. J. W. O'H. Tobin, Constance M. Ormrod, * and M. R. Mullins.

* In absence.

University of Cambridge

At recent examinations the following were successful :

DMRE

Part I.—Olga Bauerova, Phyllis Burvill-Holmes, Francis Freund, Benzion Kounine, Arnost Preiss, and Ernst Rachwalsky.

Part II.—G. K. F. Cohen, R. M. Crichton, Timothy Culloty, Francis Freund, Maria E. Grossman, H. T. Halper, H. R. C. Hay, C. J. C. G. Hodson, D. A. Jennings, M. B. Leitch, J. M. Mennell, D. J. Mitchell, R. G. Moffat, J. Y. Rabinowitch, Katharina Rosenkranz, A. W. Simmins, J. H. Smitham, and Lilian H. Walter.

University of London

Mr. B. W. Windeyer has been appointed to the new chair of radiology at Middlesex Hospital medical school (see the *Lancet*, 1942, i, 508).

Mr. Windeyer graduated from the University of Sydney in 1927, obtaining the Edinburgh surgical fellowship three years later. He took the DMRE in 1934 and was elected to the fellowship of the Faculty of Radiologists in 1940. He has been on the staff of the Middlesex Hospital since 1931, and in 1937 was appointed medical officer in charge of the Meyerstein Institute of Radiotherapy. His published work includes papers on the use of radiotherapy in urology and in non-malignant uterine hæmorrhage.

Mr. F. G. Young, DSc, a member of the scientific staff of the Medical Research Council, has been appointed to the chair of biochemistry at St. Thomas's Hospital medical school, and Mr. Alexander Lawson, PhD, lecturer in chemistry at University College, Southampton, has been appointed to the readership in organic chemistry at the London (R.F.H.) School of Medicine for Women.

Scottish Conjoint Board

At recent examinations of the board of the Royal Colleges of Physicians and Surgeons of Edinburgh, and the Royal Faculty of Physicians and Surgeons of Glasgow the following were successful :

LRCP & SE, LRFP & S

G. E. Barnard, K. H. Bayatti, W. L. Bilsland, William Brydone, B. H. Budoff, R. S. David. A. R. N. Dhanji, Jess Diamond, E. S. M. Douglas, M. R. El Sarraff, A. H. Esmat, M. S. A. El Hamid, C. C. Haupt, El S. A. K. Himmat, P. S. Huck, C. L. Isitt, H. E. Katz, Ian McKechnie, Robert Mitchell, L. E. Mosscrop, M. A. Motagalli, A. C. Muir, J. A. Murdoch, J. A. M. Ratcliffe, Harold Rosenberg, Albert Schmookler, Monroe Schneider, J. S. Seaton, S. P. Selvadurai, J. K. K. Stielau, Bernard Stillerman, Seymour Tenzer, I. A. M. Thomson, Ramapillai Vannithamby, Harry Walker and Isidor Wolff.

Manfred Gross, MD Berlin, as graduate of a recognised foreign university, was also admitted a licentiate.

Royal College of Surgeons of Edinburgh

At a meeting of the college on July 23, with Mr. J. W. Struthers, the president, in the chair, the diploma of honorary fellowship was presented to Lieut.-General Alexander Hood, DG AMS, and to Prof. A. T. Jurasz, dean of the Polish Medical Faculty of the University of Edinburgh. The following were admitted to the fellowship :

George Bankoff, MD Florence ; Hassan Din, MB Punjab ; T. J. Evans, MB Lond. ; Dora J. B. Falconer, MRCS ; A. P. Gracie, MB Edin. ; J. D. Hallissy, MB NUI ; A. W. Kay, MB Glasg. ; G. R. Nicks, MB NZ ; D. L. Savill, MB Edin. ; J. A. E. Watts, MRCS ; and E. B. Wild, MRCS.

Glasgow Smallpox Epidemic

Up to July 10 there were 39 confirmed cases of smallpox in Glasgow, including 10 cases from the ship. There were no further cases until July 20 when one was discovered in a mental hospital. On July 21 a Glasgow girl, holidaying in London, was admitted to hospital there as a case of smallpox. On July 24 a further case was diagnosed in Argyllshire. There have been 7 deaths among these 42 patients.

Royal Medical Benevolent Fund

At a quarterly council meeting on July 28 Sir Arnold Lawson, who was re-elected chairman, said that his personal letter sent out with the report had got in more subscribers and increased the number paying by banker's order. Several new legacies were announced. Figures submitted by the secretary showed that the total book-value of investments, the amount of money distributed annually, the subscription income, and the dividend income, had all been doubled during the last 15 years. During the same period the working expenses had only gone up from £1428 in 1927 to £1617 in 1941. The case committee reported the growing difficulties of beneficiaries in these days of higher living expenses. The unwritten rule to give no grant to anyone with an income of over £100 may have to be relaxed. The secretary would impress expectant testators with the need for accurate terminology ; their bequests are frequently so worded as to make it difficult to decide to what body the legacy was left. The ambiguity may sometimes nullify the legacy. It was decided that in future new applicants need not obtain the supporting signature of a subscriber ; the recommendation of any medical practitioner will be enough.

More Approved Names for Drugs

The General Medical Council has approved names for three more substances now being produced, or likely shortly to be produced, by British manufacturers.

Approved names	*Previous names*
Dienœstrol	Di-*p*-hydroxyphenylhexadiene
Pheniodol	Biliselectan
Ethisterone	Ethinyltestosterone, Pregneninolone, Lutocyclin, Progestoral, Lutogyl, Proluton C

The question of including these substances in the British Pharmacopœia is under consideration.

A new Portugese medical journal called *Amatus Lusitanus* is designed to carry on the tradition of Portuguese medicine set by Amato Lusitano, a worthy contemporary of Andreas Vesalius and Ambroise Paré. The first issue contains a well-illustrated article on the structure and functions of the hypophysis by A. C. da Costa ; a study by J. Cutileiro of the types of pneumococci found in 69 cases of lobar pneumonia and the relation between the type of infection and the symptoms and prognosis ; a lecture on malaria by F. J. C. Cambournac ; and a report of a case of acute pemphigus by J. Esteves. The general standard is high. An English summary of each article would increase the value of the journal to most English readers ; only one article in the first number has such a summary.

ERRATUM.—In the letter on " Dangers of Dulcin " (p. 141 of our last issue, 11th line from end), for rapidly read *sapidly*.

The fact that goods made of raw materials in short supply owing to war conditions are advertised in this paper should not be taken as an indication that they are necessarily available for export.

Births, Marriages and Deaths

BIRTHS

CURRAN.—On July 21, at Wolverhampton, the wife of Dr. T. P. Curran, of Stafford—a daughter.

ELLIS JONES.—On July 27, at Woking, the wife of Surgeon Lieutenant E. Ellis Jones, RNVR—a daughter.

JOHNSTON.—On Aug. 1, in London, the wife of Dr. Colin McKie Johnston, BDS—a son.

RUSSELL.—On July 24, at Oxford, the wife of Major W. Ritchie Russell, RAMC, of Edinburgh—a daughter.

MARRIAGES

MILNE—MCKENDRICK.—On July 25, at Beaconsfield, Frank A. Milne to Margaret Elizabeth McKendrick, MRCS.

DEATHS

ASTON.—On July 29, at Seaview, Isle of Wight, Richard Norman Aston, MRCS.

BUCKHAM.—On July 31, at Hereford, Frederick Buckham, LRCP, formerly of Cardiff, aged 94.

DREWITT.—On July 29, in London, Frederic George Dawtrey Drewitt, MD OXFD, FRCP, aged 94.

FRASER.—On July 27, at Caistor, Lincolnshire, Alexander Fraser, MB EDIN., JP.

NEISH.—On July 27, at Tunbridge Wells, William Alexander Neish, MB GLASG.

TALLACK.—On Aug. 1, John Reginald Arthur Tallack, MB LPOOL, of Grays, Essex, aged 40.

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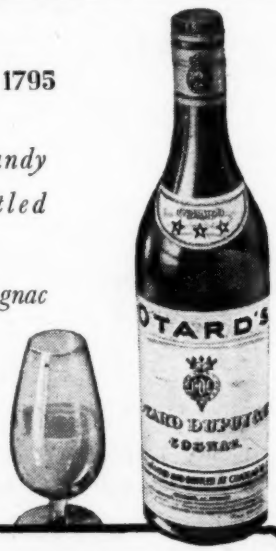

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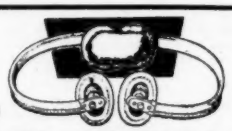
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Students beginning the clinical course spend the first clinical year at the Annexe at Brentwood under the Honorary Staff of the London Hospital. After a year of clinical experience in the wards they move to the laboratories of Chase Farm Hospital at Enfield for a course in Pathology, given by the Pathologists to the London Hospital. During this course, students are taken to Claybury Mental Hospital for a course in Mental Diseases and to the Eastern Fever Hospital for a course in the Acute Fevers. After the course in Pathology, students are sent for six months to gain experience as Student House Officers (free board and lodging and a salary of £50 a year) or as E.M.S. Dressers (free board and lodging) at Sector Hospitals. During the third clinical year, all students return to the London Hospital for clinical work in the wards and Out-patient Departments and for systematic lectures in preparation for the Final Examinations. Twelve students live in the London Hospital free of charge as Emergency Dressers. Others can live at home or at the nearby County Council Hospitals (many as E.M.S. Dressers) and come to the Hospital every day.
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L. M. S. S. A.

FINAL EXAMINATION: SURGERY, October 12th, November 9th, December 7th, 1942; MEDICINE, October 19th, November 16th, December 14th, 1942; MIDWIFERY, October 20th, November 17th, December 15th, 1942.
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This beautiful mansion situated in the heart of the country (less than two hours from London by L.M.S.R.) and surrounded by charming pleasure grounds in which games and outdoor occupational therapy are available is devoted to the treatment of Alcoholism and "Nerves" by psychotherapeutic and ancillary methods.
Illustrated Brochure and particulars obtainable from A. E. CARVER, M.D., D.P.M., Resident Medical Superintendent.

TOR-NA-DEE SANATORIUM
Managing Director: DAVID LAWSON, M.D., F.R.S.E.
FOR THE TREATMENT OF PULMONARY TUBERCULOSIS AND ALLIED DISEASES
Medical Superintendent: R. Y. KEERS, M.D. (Edin.)
For prospectus apply to The Secretary, Tor-na-Dee, Murtle, Aberdeenshire **Telephone: Cults 107**

CRICHTON ROYAL, DUMFRIES
FOR NERVOUS AND MENTAL DISORDERS
Cases of Alcoholism and Drug Addiction are admitted. Every facility for individual treatment on the most modern lines **Special Department for Insulin Therapy.** Fully equipped Gymnasium, Golf Course, and Indoor Swimming Pool. Specially trained Occupational and Recreational Therapists.
Medical Certificates given anywhere in the British Isles are valid for admission of patients.
Physician Superintendent: **P. K. McCOWAN**, J.P., M.D., F.R.C.P., D.P.M., Barrister-at-Law. *Telephone:* Dumfries 1119.

THE CASSEL HOSPITAL
FOR FUNCTIONAL NERVOUS DISORDERS
new address: ASH HALL, BUCKNALL, near STOKE-on-TRENT, STAFFS *Telephone:* **ASH BANK 215**
Temporarily removed from Swaylands, Penshurst, Kent, to above country house about five miles from Stoke in the direction of Ashbourne.
The Hospital will continue to admit for treatment patients of moderate means suffering from psychoneurotic illnesses.
Patients suffering from psychotic illnesses are not eligible for admission.
Further particulars may be obtained by application to the Medical Director at the new address.

COURT HALL, KENTON, near EXETER
FOR THE TREATMENT OF EIGHT LADIES, VOLUNTARY, TEMPORARY AND CERTIFIED PATIENTS
CLIFFDEN, TEIGNMOUTH
FOR EARLY AND CONVALESCENT CASES Recreational Therapies are held daily by skilled Leaders
The house stands high with spacious balconies and extensive views of the South Devon Coast. Beautiful garden. Own Dairy in 25 acres. Private road to beach
There is also a charming house, **EBWORTHY, MANATON, DARTMOOR**, situated in 20 acres, 1100 ft. up for bracing moorland air
Resident Physicians—BERTHA M. MULES, M.D., B.S. ANNE S. MULES, M.R.C.S., L.R.C.P. *Telephones*—STARCROSS 259 and TEIGNMOUTH 289

PECKHAM HOUSE, 112, Peckham Road, London, S.E.15
Telegrams: "Alleviated, London" **Telephone: Rodney 2641-2642**
A Private Mental Hospital, for Ladies and Gentlemen suffering from Nervous and Mental Illness, where the amenities of a comfortable home are combined with full investigation and every well-established modern treatment.
Terms from 3½ guineas weekly.
Illustrated Prospectus may be obtained from the Physician Superintendent.

THE COTSWOLD SANATORIUM
On the Cotswold Hills seven miles from Cheltenham, Stroud and Gloucester. Fully equipped for the treatment of all forms of Tuberculosis. **Terms: 5½ to 9½ guineas per week, inclusive.** Full particulars from MEDICAL SUPERINTENDENT, Cotswold Sanatorium, Cranham, Gloucester. *Telephone:* Witcombe 81. *Telegrams:* "Hoffman, Birdlip."

ST. ANDREW'S HOSPITAL FOR NERVOUS AND MENTAL DISORDERS

NORTHAMPTON

FOR THE UPPER AND MIDDLE CLASSES ONLY.

PRESIDENT: THE MOST HON. THE MARQUESS OF EXETER, K.G., C.M.G., A.D.C.

MEDICAL SUPERINTENDENT: THOMAS TENNENT, M.D., F.R.C.P., D.P.H., D.P.M.

This Registered Hospital is situated in 130 acres of park and pleasure grounds. Voluntary patients, who are suffering from incipient mental disorders or who wish to prevent recurrent attacks of mental trouble; temporary patients, and certified patients of both sexes are received for treatment. Careful clinical, bio-chemical, bacteriological, and pathological examinations. Private rooms with special nurses, male or female, in the Hospital or in one of the numerous villas in the grounds of the various branches can be provided.

WANTAGE HOUSE

This is a Reception Hospital in detached grounds with a separate entrance, to which patients can be admitted. It is equipped with all the apparatus for the complete investigation and treatment of Mental and Nervous Disorders by the most modern methods: insulin treatment is available for suitable cases. It contains special departments for hydrotherapy by various methods, including Turkish and Russian baths, the prolonged immersion bath, Vichy Douche, Scotch Douche, Electrical baths, Plombieres treatment, etc. There is an Operating Theatre, a Dental Surgery, an X-Ray Room, an Ultra-violet Apparatus, and a Department for Diathermy and High-frequency treatment. It also contains Laboratories for bio-chemical, bacteriological, and pathological research. Psychotherapeutic treatment is employed when indicated.

MOULTON PARK

Two miles from the Main Hospital there are several branch establishments and villas situated in a park and farm of 650 acres. Milk, meat, fruit, and vegetables are supplied to the Hospital from the farm, gardens, and orchards of Moulton Park. Occupational therapy is a feature of this branch, and patients are given every facility for occupying themselves in farming, gardening, and fruit growing.

BRYN-Y-NEUADD HALL

The seaside house of St. Andrew's Hospital is beautifully situated in a Park of 330 acres, at Llanfairfechan, amidst the finest scenery in North Wales. On the North-West side of the Estate a mile of sea coast forms the boundary. Patients may visit this branch for a short seaside change or for longer periods. The Hospital has its own private bathing house on the seashore. There is trout-fishing in the park.

At all the branches of the Hospital there are cricket grounds, football and hockey grounds, lawn tennis courts (grass and hard courts), croquet grounds, golf courses, and bowling greens. Ladies and gentlemen have their own gardens, and facilities are provided for handicrafts, such as carpentry, etc.

For terms and further particulars apply to the Medical Superintendent (TELEPHONE: No. 2356 and 2357 Northampton), who can be seen in London by appointment.

CHEADLE ROYAL CHEADLE CHESHIRE

A Registered Hospital for MENTAL DISEASES, and its Seaside Branch, GLAN-Y-DON, Colwyn Bay, N. Wales

THE object of this Hospital is to provide the most efficient means for the treatment and care of those of the Upper and Middle Classes suffering from MENTAL and NERVOUS DISEASES. The Hospital is governed by a Committee appointed by the Trustees of the Manchester Royal Infirmary.

VOLUNTARY, TEMPORARY, AND CERTIFIED PATIENTS RECEIVED

For Terms and further information apply to the MEDICAL SUPERINTENDENT *Telephone:* GATLEY 2231

CAMBERWELL HOUSE, 33, Peckham Road, London, S.E.5

Telegrams: "PSYCHOSIA, LONDON" — FOR THE TREATMENT OF MENTAL DISORDERS — *Telephone:* RODNEY 4942 (2 lines)

Completely detached Villas for mild cases. Voluntary Patients received. Twenty acres of grounds; own garden produce. Hard and grass tennis courts, putting greens, Recreation Hall with Badminton Court, and all indoor amusements. Occupational therapy, Calisthenics, Actino-therapy, prolonged immersion baths, shock and also modified insulin treatment. Chapel.

Senior Physician, Dr. HUBERT JAMES NORMAN, assisted by a resident Medical Staff and visiting Consultants

An Illustrated Prospectus giving fees, which are strictly moderate, may be obtained upon application to the Secretary

The Convalescent Branch is HOVE VILLA, BRIGHTON, and is 200 ft. above sea-level

CITY OF LONDON MENTAL HOSPITAL

Near DARTFORD, KENT.

Ladies and Gentlemen received for treatment under certificates, and without certificates as either VOLUNTARY or TEMPORARY PATIENTS, at a weekly fee of £2 9s., and upwards.

MALLING PLACE, KENT

For LADIES and GENTLEMEN of Unsound Mind.

Terms moderate. Apply to Resident Medical Superintendent. Telegrams: ADAM WEST MALLING. Telephone No. 2: MALLING.

CHISWICK HOUSE,

PINNER, MIDDLESEX.

Telephone: PINNER 234.

A Private Hospital for the Treatment and Care of Mental and Nervous Illnesses in both Sexes.

A modern country house, 12 miles from Marble Arch, in attractive and secluded surroundings. Fees from 10 guineas per week inclusive. Cases under Certificate, Voluntary and Temporary Patients received for treatment.

DOUGLAS MACAULAY, M.D., D.P.M.

THE COPPICE, NOTTINGHAM

HOSPITAL FOR MENTAL DISEASES

President: The Right Hon. LORD BELPER

REGISTERED HOSPITAL for Voluntary, Temporary, or Certified PRIVATE PATIENTS of UPPER and MIDDLE CLASSES. Own kitchen garden. Modern forms of treatment, including Electro-shock Therapy. Out-door games, cinema visits, motor drives arranged. Visiting Chaplain.

For terms, &c., apply to: Dr. G. M. WODDIS, Medical Superintendent. Telephone: 64117 Nottingham.

FENSTANTON at "FIVE DIAMONDS," Chalfont St. Giles, Bucks

A Private Home for the Care and Treatment of a limited number of LADIES with Mental and Nervous Disorders. Certified, Voluntary, and Temporary Patients received. Mansion with 12 acres of ground. (See *Medical Directory*, p. 2362.) Apply Resident Physician. Telephone: Little Chalfont 2046. Station: Chalfont and Latimer.

HEIGHAM HALL, NORWICH

PRIVATE MENTAL HOME for Nervous and Mental Illness. All forms of treatment available. Fees from 4 gns. per week upwards according to requirements. Vacancies occasionally exist at reduced fees on the recommendation of the patient's own physician.

Apply to Dr. J. A. SMALL. Telephone: Norwich 20099

London Hospital, E.1.

Applications are invited for the post of RADIO-THERAPIST. The successful candidate will be required to organise and take charge of the new department Radio Therapy. Salary £1500 per annum. Private practice to be allowed only in the hospital on an agreed basis.

Applications, together with testimonials, should be sent to the House Governor (from whom further particulars of the appointment may be obtained) and should arrive not later than Tuesday, 8th September.

H. BRIERLEY, House Governor.

London County Council.

Registered medical practitioner required as Part-time MEDICAL OFFICER at MILE OAK APPROVED SCHOOL, PORTSLADE, SUSSEX. Duties include attendance at the school at least once every week, and at such other times as may be necessary. Candidates must reside within easy reach of the school. The appointment is temporary and subject to review at any time, in any case by the end of the war. Salary in accordance with the accommodation of the school; on present figures £75 a year.

Application forms obtainable (stamped addressed foolscap envelope) from EDUCATION OFFICER (S.S.5.), County Hall, Westminster Bridge, S.E.1, and must be returned by 20th August, 1942.

UNIVERSITY EXAMINATION POSTAL INSTITUTION

17, RED LION SQUARE, LONDON, W.C.1

Over 50 years' experience

POSTAL COACHING FOR ALL MEDICAL EXAMINATIONS

MEDICAL PROSPECTUS (36 pages)

sent gratis, along with List of Tutors, &c., on application to the Principal, 17, Red Lion-square, London, W.C.1. (Telephone: HOLborn 6818.)

The South London Hospital for Women,

Clapham Common, S.W.4.

Applications are invited from medical Women for the following appointments: HOUSE PHYSICIAN (A) and SECOND HOUSE SURGEON (A), for a period of six months from 1st September. Salary in both cases at the rate of £100 per annum, with full residential emoluments. W practitioners liable under the National Service Acts, 1939–41, may apply.

Applications, stating age, nationality, qualifications with dates, and accompanied by copies of three recent testimonials, should be sent to the SECRETARY at the Hospital by Saturday, 15th August.

The Royal National Throat, Nose and

EAR HOSPITAL, Gray's Inn-road, W.C.1.

Applications are invited from registered medical practitioners, Male or Female, for the appointment of RESIDENT HOUSE SURGEON (B2), to become vacant shortly. Practitioners who have been qualified more than three months and liable under the National Service Acts, 1939–41 (males cannot be considered unless rejected by the R.A.M.C.), may also apply when appointment will be limited to six months; otherwise for a period of nine months. The salary is at the rate of £100 per annum, with full residential emoluments.

Applications should be sent as soon as possible to—

JOHN H. YOUNG, Secretary-Superintendent.

Queen Mary's Hospital for the East

END, E. 15.

Applications are invited for an HONORARY ORTHOPÆDIC SURGEON to the above Hospital. The appointment, which is in the first instance for the duration of the war, necessitates one out-patient session a week, and the supervision of the fracture clinic.

Candidates must be Fellows of a Royal College of Surgeons engaged in Consulting Practice.

Application to be sent forthwith to—

BERNARD T. HEMPEL, Captain, Chairman.

University of London.

The Senate invite applications for the UNIVERSITY CHAIR OF CHEMISTRY tenable at the ROYAL CANCER HOSPITAL. Salary £1000 a year. Applications (ten copies) must be received not later than first post on Tuesday, 1st September, 1942, by the ACADEMIC REGISTRAR, University of London, Richmond College, Richmond, Surrey, from whom further particulars should be obtained.

Borough of Walthamstow.

APPOINTMENT OF DEPUTY MEDICAL OFFICER AND DEPUTY SCHOOL MEDICAL OFFICER (TEMPORARY).

The Council invites applications from Male medical practitioners for the above appointment at a commencing salary of £750 per annum, rising by annual increments of £25 to £800 per annum, plus cost-of-living bonus and car mileage allowance. The appointment will be for the period of absence on service of the present holder of the appointment. Candidates for the appointment must hold a registrable qualification in public health and school medicine, and must have had at least three years' previous experience in all branches of public health and school medical work. The appointment will be subject to the provisions of the Local Government Superannuation Act, 1937, to the Council's sick pay scheme, and to other conditions relative to staff appointments, and the successful candidate will be required to pass a medical examination.

Application must be made on the approved form, which can be obtained from the undersigned, and applications, endorsed "Deputy Medical Officer of Health," must be received by the undersigned by NOON on Saturday, 15th August, 1942.

Canvassing, either directly or indirectly, will be deemed a disqualification, and candidates must disclose in writing whether, to their knowledge, they are related to any member of or holder of any senior office under the Council. A candidate who fails to do so will be disqualified, and if appointed will be liable to dismissal without notice. FRANCIS G. GARNER, Town Clerk.

Town Hall, Walthamstow, E.17, 22nd July, 1942.

The King George Hospital, Ilford.

Applications are invited for the post of TEMPORARY HONORARY ANÆSTHETIST for the duration of the war.

Applications should be sent not later than Monday, 24th August, to: G. A. HEPWORTH, Secretary and Superintendent.

Examining Surgeons:

FACTORIES ACT, 1937.

The following appointment as Examining Surgeon under the Factories Act, 1937, is vacant.

Applications should be sent to the CHIEF INSPECTOR OF FACTORIES, 28, Broadway, London, S.W.1.

District	*County*	*Latest date for receipt of application*
SADDELL AND SKIPNESS ..	ARGYLL ..	18th August, 1942.

Central London Ophthalmic Hospital,

Judd-street, W.C.1.

Applications are invited from registered medical practitioners, Male and Female, for the appointment of RESIDENT HOUSE OFFICER (B2). Practitioners qualified more than three months and liable under the National Service Acts, 1939–41 (males must be rejected by the R.A.M.C.) may also apply, when appointment is limited to six months. The successful candidate will be afforded ample opportunity to study for the D.O.M.S.

Applications, with copies of three testimonials, to be sent immediately to— FRANK HART, Secretary.

East Ham Memorial Hospital,

Shrewsbury-road, E.7.

Applications are invited from registered medical practitioners (Male and Female) for the following appointments, to become vacant on 22nd August:—

HOUSE SURGEON AND CASUALTY OFFICER (A), including practitioners within three months of qualification and liable under the National Service Acts, 1939–41, when appointment will be for six months. Salary is at the rate of £120 per annum, with full residential emoluments.

HOUSE PHYSICIAN (B2). Practitioners qualified more than three months and liable under the National Service Acts, 1939–41 (males must be rejected by the R.A.M.C.), may also apply, when appointment will be limited to six months. Salary is at the rate of £200 per annum, with full residential emoluments.

Applications, stating full particulars, accompanied by copies of three testimonials, should be forwarded immediately to—

REGINALD PERRY, Secretary-Superintendent.

County Borough of Tynemouth.

SOCIAL WELFARE COMMITTEE.
PRESTON HOSPITAL, NORTH SHIELDS.

ASSISTANT MEDICAL OFFICER (A) (NON-RESIDENT).

Applications are invited from registered medical practitioners, Male and Female, for the above-mentioned post (which will be vacant on 14th October, 1942), including practitioners within three months of qualification and liable under the National Service Acts, 1939–41, when appointment will be for six months; otherwise for twelve months. The salary will be £250 per annum, plus emoluments to the value of £100 per annum. The officer appointed will be required to refund to the Council all fees received. The appointment will be subject to one month's notice on either side. The appointment is a whole-time one and the officer appointed will be required to submit a satisfactory medical certificate, and to act under the direction of the Medical Officer.

Applications, stating age, experience, qualifications, nationality, and date able to begin duty, accompanied by not more than three recent testimonials, and endorsed "Assistant Medical Officer," must be delivered to the undersigned not later than 31st August. Further information may be obtained from the Medical Officer, Preston Hospital, North Shields.

Canvassing, either directly or indirectly, will be a disqualification. FRED G. EGNER, Town Clerk.

14, Northumberland-square, North Shields,
31st July, 1942.

King Edward VII Hospital, Windsor.

Applications are invited from registered medical practitioners Male and Female, for the appointment of a HOUSE SURGEON (A), to become vacant at the end of August, including practitioners within three months of qualification who are liable to service under the National Service Acts, 1939–41. If held by a practitioner who is liable under these Acts, appointment will be for a period of six months. Salary is at the rate of £120 per annum, with full residential emoluments.

Applications should be sent to the SECRETARY not later than 18th August, together with copies of recent testimonials.

University of Birmingham.

MENTAL DISEASE RESEARCH DEPARTMENT.

Applications are invited for the appointment of ASSISTANT to the Chief Research Officer. Histological experience essential. Preferably medically qualified. British. Salary £450 per annum.

Applications by 1st September to: C. G. BURTON, Secretary.

Royal Earlswood Institution for

MENTAL DEFECTIVES, REDHILL, SURREY.

ASSISTANT MEDICAL OFFICER (Male) required, single, British (B1 post). R practitioners holding A or B2 posts and rejected by the R.A.M.C. may also apply. Salary £450 per annum, board-residence provided.

Apply MEDICAL SUPERINTENDENT, and enclose two references.

HIS MAJESTY'S COLONIAL SERVICE

THE COLONIAL MEDICAL SERVICE

VACANCIES FOR MEDICAL OFFICERS

The maintenance of an efficient Colonial Medical Service constitutes a vital part of the national war effort and it is most important that the Service should be assured of an adequate supply of doctors.

The Secretary of State for the Colonies therefore invites applications from doctors possessing a medical qualification registrable in the United Kingdom who are British subjects and who are under thirty-five years of age.

Medical Officers are appointed in the first instance for general service. But there are ample opportunities for work in special branches of medicine and surgery, in public health and in medical research.

The normal salary scale is from £600 to between £1,000 and £1,120. There are large numbers of super-scale posts to which promotion is made on merit and which carry higher salaries.

Government quarters, in many cases free of rent, and first-class passages to and from the Colonies are provided, and an adequate pension scheme is in force.

Selected candidates are normally required to attend a course of instruction in Tropical Medicine and Hygiene either before proceeding overseas or during their first period of leave.

Further particulars, including the regulations governing admission to the Colonial Medical Service, may be obtained from the Director of Recruitment (Colonial Service), 2, Park-street, London, W.1.

Leicester Royal Infirmary.

VACANCIES, 1ST OCTOBER, 1942.

FOUR HOUSE SURGEONS (A).

Applications are invited from registered medical practitioners, Male and Female, including practitioners within three months of qualification who are liable to service under the National Service Acts, 1939–41. Salary at the rate of £125 per annum.

HOUSE PHYSICIAN (B2). Salary £125 per annum.

RESIDENT ANÆSTHETIST (B2). First six months £150 per annum, second six months £200 per annum, third six months £250 per annum.

All appointments with full residential emoluments.

Applications are invited from registered medical practitioners, Male and Female. Male practitioners qualified more than three months cannot be considered unless rejected by the R.A.M.C. To practitioners, Male or Female, liable under the National Service Acts, 1939–41, the appointments will be for six months.

Applications to be forwarded to HOUSE GOVERNOR AND SECRETARY on or before 15th August.

30th July, 1942.

Glamorgan County Council.

Applications are invited for the post of COUNTY MEDICAL OFFICER and SCHOOL MEDICAL OFFICER for the County of Glamorgan. Candidates must possess high medical qualifications and hold a Diploma in Public Health. They should preferably have held the post of Medical Officer of Health (or Deputy) in a County or County Borough; have had experience in hospital administration and the work included in the scope of a Public Health Committee, an Education Committee, a Public Assistance Committee and an Emergency Committee for Civil Defence purposes. The Medical Officer of Health may be required to take part in teaching in accordance with any agreement which may be made between the County Council and the Welsh National School of Medicine. Candidates must not be less than thirty and not more than forty-five years of age. The latter age may be relaxed in the case of a specially suitable candidate employed by a Local Authority. The post is superannuable and the appointment is subject to the successful candidate passing a medical examination. The salary offered is £1400 per annum inclusive, with travelling and personal expenses on the County Scales.

Further particulars of duties and terms of appointment may be obtained from the undersigned, to whom all applications must be sent, accompanied by copies of three testimonials, not later than 24th August, 1942.

Canvassing directly or indirectly will disqualify.

HENRY ROWLAND, Clerk of the County Council.

Glamorgan County Hall, Cardiff, 30th July, 1942.

Nottingham and Midland Eye INFIRMARY.

Applications are invited from registered medical practitioners, Male and Female, for the appointment of a HOUSE SURGEON (B1). Applicants should have had some surgical ophthalmic experience. R practitioners holding A or B2 posts and rejected by the R.A.M.C. may also apply. Salary at the rate of £200, with full residential emoluments.

Applications, stating age, nationality, qualifications, and experience, with copies of three recent testimonials, immediately to— T. RUSSELL MOORE, Secretary.

The Ropewalk, Nottingham.

Burton-on-Trent General Infirmary.

Applications are invited from registered medical practitioners (Male) for the appointment of CASUALTY OFFICER and HOUSE PHYSICIAN (A), including practitioners within three months of qualification and liable under the National Service Acts, 1939–41, when appointment will be for six months. Salary at the rate of £150 per annum, with usual emoluments.

Applications, stating age, qualifications with dates, and nationality, and accompanied by copies of three recent testimonials, to be sent to—

E. W. THORNLEY, Superintendent and Secretary.

Coldeast Colony, Sarisbury Green, Near SOUTHAMPTON.

Applications are invited from registered medical practitioners, Male and Female, for the appointment of ASSISTANT MEDICAL OFFICER (B2) at the above Mental Deficiency Institution, which is situated about seven miles from Southampton. Practitioners qualified more than three months and liable under the National Service Acts, 1939–41 (males must be rejected by the R.A.M.C.), may also apply, when appointment is limited to six months. Salary £350 per annum rising by £25 annually to £450, with an additional annual payment of £50 for being in possession of the D.P.M., and full residential emoluments, valued for superannuation purposes at £150 per annum. The duties of the appointment would include assisting at the Ministry of Health Hospital attached to the Colony, as required. The appointment is subject to the provisions of the Asylums and Certified Institutions (Officers Pensions) Act, 1918, and the successful candidate would be required to pass a satisfactory medical examination.

Applications, stating age, qualifications with dates, nationality, and present post, and accompanied by copies of three recent testimonials, should be sent not later than first post on 15th August, 1942, to— A. WILSON, Medical Superintendent.

City of Birmingham.

MATERNITY AND CHILD WELFARE DEPARTMENT,

The Public Health Committee invite applications from qualified medical Women to act as TEMPORARY ASSISTANT MEDICAL OFFICER at the CITY MATERNITY HOME, 134, Heathfield-road, Handsworth. The Home is a Second Certificate training school for midwives, with 40 Beds. Applicants should have had considerable experience in practical obstetrics. The work includes attendance at antenatal and children's clinics. The post is non-resident, and the salary scale is £500 rising by £25 annually to £700 per annum, plus bonus; the commencing salary within that scale depends on the medical officer's experience.

Applications, endorsed "Medical Officer for Maternity and Child Welfare" and accompanied by copies of three testimonials, to be made on a form obtainable from the MEDICAL OFFICER OF HEALTH, Council House, Birmingham, 3, and returned to him on or before 22nd August, 1942.

Corporation of Aberdeen.

PUBLIC HEALTH SERVICES—BACTERIOLOGICAL DEPARTMENT.

Applications are invited for the post of ASSISTANT CLINICAL PATHOLOGIST to the Corporation of Aberdeen. The post is temporary for the duration of the war. The post is non-resident. For those with considerable experience in Clinical Pathology in its various aspects, the salary will be at the rate of £500 per annum, with annual increments of £25 on approved service to £700 per annum. The Conditions of Service shall be as laid down by the Corporation from time to time.

Applications, stating age and experience, and accompanied by four copies of three recent testimonials, should be submitted not later than Tuesday, 25th August, 1942, to—

HARRY J. RAE, Medical Officer of Health.

City Health Department, 4, Albyn-place, Aberdeen.

City and County of the City of LINCOLN.

Applications are invited for the appointment of ASSISTANT MEDICAL OFFICER OF HEALTH from Male and Female candidates. The duties of the post relate mainly to Maternity and Child Welfare. Salary £500–£25–£700 plus cost-of-living bonus according to scale. Commencing salary according to experience.

Applications must be made on the prescribed form not later than 24th August, 1942. Forms of application and further particulars of appointment may be obtained from the Medical Officer of Health, Beaumont Fee, Lincoln.

J. H. SMITH, Town Clerk.

Corporation Offices, Lincoln, 1st August, 1942.

City of Manchester.

PUBLIC HEALTH DEPARTMENT.

CRUMPSELL HOSPITAL (1400 Beds) and WITHINGTON HOSPITAL (1150 Beds).

The Public Health Committee invite applications for the appointments of TEMPORARY VISITING CONSULTANT DERMATOLOGISTS (part-time) at the Crumpsall Hospital, Manchester, 8, and at the Withington Hospital, Manchester, 20. The appointments will be for the period of the war. They are part-time and do not carry with them right of entry into the Corporation Superannuation Fund. The salary for each appointment will be at the rate of £125 per annum, and application may be made for either or both of the posts.

Forms of application and copies of a memorandum of the terms and conditions of the appointments may be obtained from the Medical Officer of Health, Hospitals Administration Section, Box No. 399, Town Hall, Manchester, 2, by whom all applications must be received on or before 20th August, 1942. Canvassing in any form is prohibited.

R. H. ADCOCK, Town Clerk.

Town Hall, Manchester, 2, 23rd July, 1942.

Great Barr Park Colony

AND HOSPITAL, BIRMINGHAM, 22A.

Applications are invited from registered medical practitioners, Male and Female, for the appointment of ASSISTANT RESIDENT MEDICAL OFFICER (A), now vacant, including practitioners within three months of qualification and liable under the National Service Acts, 1939–41, when appointment will be for a period of six months. Salary is at the rate of £275 per annum, with full residential emoluments, plus war bonus.

Applications, stating age, qualifications with dates, and nationality, and accompanied by copies of three recent testimonials, should be sent to the MEDICAL SUPERINTENDENT, Great Barr Park Colony, Birmingham, 22A.

The Royal Liverpool United Hospital.

DAVID LEWIS NORTHERN HOSPITAL.

Applications are invited from registered medical practitioners, Male and Female, for the B1 appointment of RESIDENT ASSISTANT SURGEON, duties to commence immediately. Applicants should have held house appointments and had surgical experience. Preference will be given to candidates holding diploma of F.R.C.S. R practitioners holding A or B2 posts cannot be considered unless rejected by the R.A.M.C. Salary is at the rate of £350 per annum, with board and lodging.

Applications, stating age, nationality, qualifications, with experience and details of previous appointments, and (except in the case of students of the Liverpool Medical School) accompanied by copies of three recent testimonials, should be sent not later than Tuesday, 25th August, 1942, to—

A. V. J. HINDS, Secretary.

The Royal Liverpool United Hospital,
60, Rodney-street, Liverpool, 1, 8th August, 1942.

City of Manchester.

BOOTH HALL HOSPITAL FOR CHILDREN. (760 Beds.)

Applications are invited from registered medical practitioners, Male and Female, for the appointment of RESIDENT SURGICAL OFFICER (B1) at the above-mentioned class 1 M.S. hospital which is vacant now.

Candidates must have practical surgical experience and, preferably, hold a higher surgical qualification. Applications from male R practitioners now holding A or B2 posts cannot be considered unless rejected by the R.A.M.C.

Salary, on scale in accordance with the Manchester Corporation conditions of service, commencing at £400 per annum, rising by annual increments of £25 to a maximum of £450, together with full residential emoluments. The salary is subject to a temporary cost-of-living award. The commencing cash remuneration at present is £416 13s. 3d.

Full information and forms of application may be obtained from the Medical Officer of Health, Hospitals Administration Section, Box No. 399, Town Hall, Manchester, 2, and applications for the post must be received by him not later than 17th August, 1942.

Canvassing in any form is prohibited.

R. H. ADCOCK, Town Clerk.

Town Hall, Manchester, 2, 30th July, 1942.

City of Manchester.

BOOTH HALL CHILDREN'S HOSPITAL, MANCHESTER, 9.

LOCUM TENENS RESIDENT SURGICAL OFFICER required immediately. Salary 10 guineas weekly.

Application, giving usual details, should be made to the MEDICAL SUPERINTENDENT.

The Duchess of York Hospital for

BABIES, MANCHESTER. (80 Cots.)

Applications are invited for the post of JUNIOR RESIDENT MEDICAL OFFICER (A), including practitioners within three months of qualification and liable under the National Service Acts, 1939–41, for six months from 1st October, 1942. Salary at the rate of £100 per annum, with full residential emoluments.

Applications, accompanied by copies of three recent testimonials, to be sent by the 24th August, 1942, to—

LOUISE GILLESPIE, Secretary.

Staffordshire County Council.

HOSPITAL SCHEME—SEDGLEY HOSPITAL.

APPOINTMENT OF RESIDENT MEDICAL OFFICER (B2).

Applications are invited from Women registered medical practitioners for the above-mentioned appointment. W practitioners qualified more than three months and liable under the National Service Acts, 1939–41, may also apply when appointment is limited to six months; otherwise will not exceed twelve months. Salary is at the rate of £200 per annum, with full residential emoluments. The appointment will be of a temporary nature, subject to one month's notice on either side.

Applications, accompanied by copies of three recent testimonials, should be sent not later than the 19th August, 1942, to—

T. H. EVANS, Clerk of the County Council.

County Buildings, Stafford, 28th July, 1942.

City of Leicester.

CITY ISOLATION HOSPITAL, GROBY ROAD.

Applications are invited from registered medical practitioners for the appointment of a RESIDENT MEDICAL OFFICER (B2) at the above Hospital. Salary is at the rate of £300 per annum (plus at the present time a wartime bonus of £16 18s. per annum), with full residential emoluments. The Officer appointed may be required to assist with infant welfare work. Practitioners qualified more than three months and liable under the National Service Acts, 1939–41 (males must have been rejected by the R.A.M.C.), may also apply when appointment will be limited to six months; otherwise for not more than twelve.

Applications (on forms supplied), accompanied by copies of three recent testimonials, must be submitted as soon as possible, endorsed "R.M.O., City Isolation Hospital," and addressed to: E. K. MACDONALD, Medical Officer of Health.

Health Department, Grey Friars, Leicester, August, 1942.

Birmingham United Hospital.

THE GENERAL HOSPITAL.
THE QUEEN ELIZABETH HOSPITAL.
(Also incorporating THE QUEEN'S HOSPITAL, 1840–1941.)

Applications are invited from registered medical practitioners for the post of RADIO-THERAPEUTIC REGISTRAR (B1). Candidates must have held a senior resident post or acted as a Resident Officer for not less than twelve months. Salary £350 per annum, non-resident. R practitioners holding A or B2 posts and rejected by the R.A.M.C. may also apply.

Applications, stating age, nationality, qualifications with dates, experience, and details of previous appointments, and accompanied by copies of three recent testimonials, should be sent to the undersigned from whom all further information may be obtained.

G. HURFORD, Secretary, Birmingham United Hospital.

The Queen Elizabeth Hospital, Birmingham, 15,
29th July, 1942.

Norfolk and Norwich Hospital, Norwich.

(440 Beds.)

Applications are invited for the post of ASSISTANT PATHOLOGIST (full-time). Candidates must be registered medical practitioners with special experience in pathological work. Salary according to experience, but not less than £700 per annum.

Applications, with full particulars of experience, accompanied by copies of three recent testimonials, should be forwarded not later than first post on the 24th August to—

FRANK INCH, House Governor and Secretary.

The Royal Liverpool United Hospital,

LIVERPOOL ROYAL INFIRMARY.

Applications are invited from registered medical practitioners, Male and Female, for the appointment of FIRST ASSISTANT to the RADIOLOGICAL DEPARTMENT (B1), duties to commence immediately. Applicants should have held house appointments. R practitioners holding A or B2 posts and rejected by the R.A.M.C. may also apply. Salary is at the rate of £250 per annum.

Applications, stating age, nationality, qualifications with experience, and details of previous appointments, and (except in the case of students of the Liverpool Medical School), accompanied by copies of three recent testimonials, should be sent not later than Monday, 24th August, 1942, to—

A. V. J. HINDS, Secretary.

The Royal Liverpool United Hospital,
60, Rodney-street, Liverpool, 1.
8th August, 1942.

The Derbyshire Hospital for Women,

FRIAR GATE, DERBY (60 Beds, 18 Cots.)

Applications are invited for the post of HONORARY ASSISTANT SURGEON to the Hospital. Candidates must be qualified in accordance with the rules of the Hospital and the appointment will be subject to the limitations imposed by the war emergency conditions.

Applications for the post should be accompanied by not more than four testimonials, and four copies of both application and testimonials should be submitted not later than 24th August. Further information, if desired, may be obtained from the undersigned.

By Order,
F. T. WILTON, Superintendent and Secretary.

Middlesbrough Education Committee.

Applications are invited from duly qualified Men or Women for a temporary position as ASSISTANT SCHOOL MEDICAL OFFICER (to act whilst a permanent Officer is on war service). Commencing salary is £500 per annum (provided the successful candidate has had not less than three years' post-graduate experience), rising by annual increments of £25 to £700 per annum. The Committee will take into account previous experience as an Assistant School Medical Officer in determining the amount of the commencing salary. The successful candidate will be required to devote the whole of his/her time to the duties of the office. The successful candidate will be required to pass a medical examination. The appointment will be terminable by one calendar month's notice on either side.

Forms of application may be obtained on application to the Director of Education, Education Offices, Woodlands-road, Middlesbrough, to whom completed forms should be returned not later than Saturday, 22nd August, 1942.

Canvassing in any form will disqualify.

PRESTON KITCHEN, Town Clerk.

Town Clerk's Office, Municipal Buildings, Middlesbrough, 24th July, 1942.

Middlesbrough Education Committee.

Applications are invited from Men or Women for an appointment as a TEMPORARY ASSISTANT SCHOOL DENTAL SURGEON (to act whilst permanent officer is on war service). Applicants must hold a registered diploma or degree in Dental Surgery. The successful applicant will be required to devote the whole of his/her time to the duties of the office and to act under the direction of the School Medical Officer. Commencing salary £450 per annum, rising by annual increments of £25 to £550 per annum.

Forms of application may be obtained on application to the Director of Education, Education Offices, Woodlands-road, Middlesbrough, to whom completed forms should be returned not later than Saturday, 22nd August, 1942.

Canvassing in any form will disqualify.

PRESTON KITCHEN, Town Clerk.

Town Clerk's Office, Municipal Buildings, Middlesbrough, 24th July, 1942.

Huddersfield Royal Infirmary.

(321 Beds.)

HOUSE SURGEON (A) required to commence middle of August. Duties will include those of House Surgeon to the Abnormal Maternity Department. Salary £187 10s., with board, residence, and laundry.

ASSISTANT CASUALTY OFFICER (A) required. Duties, which include the administration of anæsthetics, to commence as early as possible. Salary £150 per annum, with board, residence, and laundry.

Practitioners within three months of qualification and liable under the National Service Acts, 1939–41, may apply when appointments will be for six months; otherwise they may be renewable.

Applications, stating age, nationality, qualifications with dates, and accompanied by copies of recent testimonials, to—

H. J. JOHNSON, General Superintendent and Secretary.

The Gloucestershire Royal Infirmary

AND EYE INSTITUTION, GLOUCESTER.

(239 Beds—Five Residents.)

Applications are invited from registered medical practitioners for the appointment of HOUSE SURGEON (A). Practitioners within three months of qualification and liable under the National Service Acts, 1939–41, may apply when appointment will be for six months; otherwise it will be for a period of six months, which may be extended for similar periods by re-election from time to time. Salary is at the rate of £150 per annum, with full residential emoluments.

Applications, stating age, qualifications with dates, and nationality, and accompanied by copies of three recent testimonials, should be sent as soon as possible to—

F. J. SYMONS, House Governor and Secretary.

23rd July, 1942.

Royal West Sussex Hospital,

CHICHESTER. (334 Beds.)

Applications are invited from registered medical practitioners for the appointment of CASUALTY OFFICER (A), vacant on 1st September, including those within three months of qualification who are liable to service under the National Service Acts, 1939–41. The appointment will be for six months, salary £120 per annum, resident. Apply not later than 17th August, 1942.

28th July, 1942. K. H. WILLIAMS, Secretary.

Weymouth and District Hospital.

Applications are invited from registered medical practitioners, Male or Female, for the appointment of SECOND HOUSE SURGEON (A) to become vacant on the 25th August, 1942, including practitioners within three months of qualification who are liable to service under the National Service Acts, 1939-41, when appointment will be for six months. Salary £140 per annum, with full residential emoluments.

Fully detailed applications, with copies of testimonials, to be addressed to the SECRETARY, Weymouth and District Hospital, as early as possible.

City of Plymouth.

CITY GENERAL HOSPITAL. (370 Beds.)

Applications are invited from registered medical practitioners, Male and Female, for the appointment of JUNIOR ASSISTANT MEDICAL OFFICER (A) at the City General Hospital, Plymouth, including practitioners within three months of qualification and liable under the National Service Acts, 1939–41, when appointment will be for six months; otherwise it will be renewable for a further six months, and is terminable by one month's notice on either side. The salary is at the rate of £250 per annum, with full residential emoluments. All fees received by the Officer must be refunded to the Council. Further details, if desired, may be obtained from the Medical Superintendent of the Hospital.

Applications, stating age, qualifications, and experience, together with copies of not more than three recent testimonials, should be sent as soon as possible to—

T. PEIRSON, Medical Officer of Health.

Seven Trees, Lipson-road, Plymouth, 23rd July, 1942.

Education Committee for the County

BOROUGH OF BRIGHTON.

APPOINTMENT OF TEMPORARY SENIOR MEDICAL OFFICER AND ASSISTANT TO THE MEDICAL OFFICER OF HEALTH.

Applications are invited for the above appointment. Candidates must have had experience of the School Medical Services, be approved by the Board of Education for Mental Deficiency work, and be able to undertake refraction work. Possession of Diploma in Public Health, or its equivalent, will be an advantage. The Officer appointed will replace an officer to be called up for Service, will act under the supervision of the Medical Officer of Health, and may be required to act as his deputy, and will be required to devote whole time to the service of the Authority. Salary £800 per annum. Canvassing, directly or indirectly, will disqualify.

Form of application and schedule of duties may be obtained from the EDUCATION OFFICER, 54, Old Steine, Brighton, 1, and must be returned by the 20th August, 1942.

The King Edward VII Welsh National

MEMORIAL ASSOCIATION.

SULLY HOSPITAL, SULLY, GLAM.

Applications are invited from registered medical practitioners, Male and Female, for the appointment of JUNIOR ASSISTANT RESIDENT MEDICAL OFFICERS (B2), two vacancies. Practitioners qualified more than three months and liable under the National Service Acts, 1939–41 (males must be rejected by the R.A.M.C.), may also apply when appointment is limited to six months; otherwise to one year. Sully Hospital has 300 Beds for patients suffering from pulmonary tuberculosis, and is provided with every facility for the diagnosis and treatment of the disease, including X-ray apparatus, major operative thoracic unit, &c. The salary is at the rate of £200 per annum, with full residential emoluments.

Applications, stating age, qualifications with dates, nationality, and present post, and accompanied by copies of three recent testimonials, should be sent immediately to—

D. A. POWELL, Principal Medical Officer.

Memorial Offices, Cathays Park, Cardiff.

Essex County Council.

ESSEX COUNTY COUNCIL HOSPITAL, BLACK NOTLEY, NEAR BRAINTREE.

Applications are invited from registered medical practitioners for the appointment of JUNIOR ASSISTANT MEDICAL OFFICER (B2) for the Sanatorium portion of the above Hospital. Applications from male R practitioners who have been qualified more than three months cannot be considered unless they have been rejected by the R.A.M.C. If held by a practitioner (Male or Female) who is liable for service under the National Service Acts, 1939–41, the appointment will be limited to six months; otherwise it will be for a period of not exceeding twelve months. The salary is at the rate of £250 per annum, with residential emoluments valued at £160 per annum.

Applications, on forms to be obtained from the undersigned, to be delivered at the County Hall, Chelmsford.

Canvassing, whether directly or indirectly, is forbidden.

JOHN E. LIGHTBURN, Clerk of the County Council.

County Hall, Chelmsford, 24th July, 1942.

The Children's Hospital, Sheffield

(INC.) (157 Beds.)

Applications are invited from registered medical practitioners, Male and Female, for the appointment of HOUSE PHYSICIAN (A) vacant 1st September, including practitioners within three months of qualification and liable under the National Service Acts 1939–41, when the appointment will be for a period of six months. Salary is at the rate of £100 per annum with full residential emoluments.

Applications, stating age, nationality, qualifications, and accompanied by three recent testimonials should be sent to the undersigned.

The successful applicant must be a member of a Medical Defence Society.

T. H. G. GARTLAND, Superintendent and Secretary.

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The Chester Royal Infirmary.

(Normal Capacity, 225 Beds.)

Applications are invited from registered medical practitioners (Male and Female) for the appointment of GENERAL HOUSE SURGEON (A), to take up duty on 1st September, including R practitioners within three months of qualification and liable under the National Service Acts, 1939–41. The appointment will be for a period of six months. The appointment is approved in connexion with the M.S. (London University) and the F.R.C.S. (England) examination. Salary is at the rate of £150 per annum, with full residential emoluments.

Applications, stating age, qualifications with dates, and nationality, and accompanied by copies of three recent testimonials, should be sent not later than 13th August, 1942, to—

W. H. GRACE, M.D., F.R.C.P.,
Honorary Secretary, Medical Committee.

City and County of Newcastle upon TYNE.

SHOTLEY BRIDGE HOSPITAL. (900 Beds.)

Applications are invited from registered medical practitioners (Male) for the appointment of RESIDENT MEDICAL OFFICER (B1). Applicants should have held previous house appointments. R practitioners holding A or B2 posts and rejected by the R.A.M.C. may also apply. The appointment is tenable for a period of twelve months, and the salary is at the rate of £450 per annum, together with full residential emoluments.

Applications, stating age, nationality, qualifications with dates, experience, and details of previous appointments, and accompanied by copies of three recent testimonials, should be sent immediately to the MEDICAL OFFICER OF HEALTH, Town Hall, Newcastle upon Tyne, 1.

Royal Western Counties Institution

(FOR MENTAL DEFECTIVES),
STARCROSS, DEVON.

Applications are invited from registered medical practitioners (Male) for the post of TEMPORARY MEDICAL OFFICER (B1). The appointment is whole time. Applicants should be exempt from liability for military service. Some previous experience of mental deficiency or psychiatry is preferable but not essential. Salary at the rate of 8 guineas per week, with apartments, board, and laundry.

Applications, stating age, nationality, qualifications, and experience, accompanied by copies of three testimonials, should be forwarded as soon as possible to the SECRETARY, The Royal Institution, Starcross.

Leigh Infirmary, Leigh, Lancs.

Applications are invited from registered medical practitioners, Male and Female, for the appointment of RESIDENT SURGICAL OFFICER (B1), to become vacant on the 1st October, 1942. Applicants should have held house appointments and had surgical experience. Preference will be given to candidates holding diploma of F.R.C.S. R practitioners holding A or B2 posts and rejected by the R.A.M.C. may apply. Salary is at the rate of £400 per annum, with full residential emoluments.

Applications, stating age, qualifications, and accompanied by copies of three recent testimonials, to be sent to—

B. R. CARTER, Secretary-Superintendent.

Royal Berkshire Hospital, Reading.

Applications are invited from registered medical practitioners, Male and Female, for the appointment of HOUSE SURGEON (A) to the GYNÆCOLOGICAL AND OBSTETRIC DEPARTMENT, which falls vacant on 1st September, 1942, including practitioners within three months of qualification and liable under the National Service Acts, 1939–41, when appointment will be for six months. Salary is at the rate of £150 per annum, with full residential emoluments.

Applications, stating age, qualifications with dates, nationality, and present post, and accompanied by copies of three recent testimonials, should be sent immediately to—

H. E. RYAN, Secretary and House Governor.

Victoria Hospital, Accrington.

Applications are invited from registered medical practitioners for the appointment of SENIOR HOUSE SURGEON (Male) (B2). Practitioners qualified more than three months and liable under the National Service Acts, 1939–41, may also apply when appointment is limited to six months. Salary £200 per annum, with full residential emoluments.

The appointment became vacant on 23rd July, 1942.

Applications should be sent as soon as possible to—

W. H. WARHURST, LL.B., Honorary Secretary.

Town Hall, Accrington.

Royal Sheffield Infirmary and Hospital.

THE ROYAL INFIRMARY, SHEFFIELD.

Applications are invited from registered medical practitioners, Male and Female, for the appointment of RESIDENT CASUALTY OFFICER (B1), now vacant. Applicants should have held house appointments and had surgical experience. R practitioners holding A or B2 posts and rejected by the R.A.M.C. may also apply. Salary is at the rate of £150 per annum.

Applications should be forwarded forthwith to—

H. KINGSLEY PEARCE,
General Superintendent and Secretary.

The Royal Infirmary, Sheffield, 6, 16th July, 1942.

University of Birmingham.

FACULTY OF MEDICINE.

The Council of the University invites applications for Two RESEARCH FELLOWSHIPS in the MENTAL DISEASE RESEARCH DEPARTMENT. The stipend offered is £750 per annum in each case, and the appointments will be made for a period of three years.

Candidates must forward their applications, together with any other credentials they may desire to offer, to reach the undersigned not later than 31st August, 1942.

G. G. BURTON, Secretary.

The University, Edmund-street, Birmingham, 3,
July, 1942.

The Guest Hospital, Dudley.

(The Resident Staff consists of a Resident Surgical Officer and Two House Surgeons.)

Applications are invited from registered medical practitioners, Male and Female, for the appointment of HOUSE SURGEON (A), vacant on the 2nd August, 1942, including practitioners within three months of qualification and liable under the National Service Acts, 1939–41, when appointment will be for six months. Salary at the rate of £200 per annum, with full residential emoluments.

Applications, stating age, qualifications with dates, and nationality, and accompanied by copies of three recent testimonials, should be sent to—

H. RAYMOND HURST, House Governor and Secretary.

21st July, 1942.

Kent County Council.

Applications are invited from medical Women to undertake part-time work in North-west Kent on a sessional basis at a fee of one and a half guineas per session, plus a travelling allowance. Applicants should have had experience in antenatal work and child welfare centres.

Applications, stating age, qualifications, and experience, to be sent to the County Medical Officer, County Hall, Maidstone.

W. L. PLATTS, Clerk of the County Council.

County Hall, Maidstone, 30th July, 1942.

Applications are invited for two posts

as Whole-time MEDICAL OFFICERS for large engineering works in London area. The senior post, involving greater responsibility and requiring wider experience, carries salary of £100 per month; salary for other post £66 13s. 4d. per month. Applicants must be over thirty-five and ineligible for military service.—Apply, with full particulars of experience, to Box No. 906, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Full-time Locum required immediately

by engineering firm employing 5000 people in Coventry—three to six months and possible permanency. Salary £650 per annum.—Write: Address, No. 907, THE LANCET Office, 7, Adam Street, Adelphi, London, W.C.2.

Doctor, many years' experience of

Venereal and Skin diseases, seeking position, either private or in hospital.—Address, No. 905, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

A Full-time Assistant Editor

(Male or Female) required immediately for scientific medical monthly. Journalistic experience and medical or scientific knowledge essential. Salary by arrangement.—Apply, giving essential details, to SECRETARY, Royal Society of Medicine, 1, Wimpole-street, W.1.

For Sale, Medical Practice, Sheffield,

house to rent; Medical Practice, Leeds, house to rent; Partnership share, best suburb, Leeds, excellent house to rent; Practice, good Panel, excellent house to rent, near Rotherham.—NATIONAL MEDICAL AGENCY, 63, Great George-street, Leeds, 1. Grams: Natmedag. Phone: 21207.

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Set of Test Lenses, Spheres (in duplicate), Cylinders, and many extras, e.g. Prisms, Maddox Rods, etc. Also, Sphygmomanometer, as new.—Dr. NOBBS, Banstead Hospital, Sutton, Surrey.

Microscope, suitable for pathological

research work, with mechanical stage, triple nosepiece, 1/12th oil immersion, 1/6th and 2/3rd objectives, substage condenser, &c., urgently required. Binocular model preferred.—Please send details to: BOOTS PURE DRUG CO., LTD., Publicity Department, Station-street, Nottingham.

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J. C. GILBERT LTD., Columbia House, Aldwych, W.C.2.
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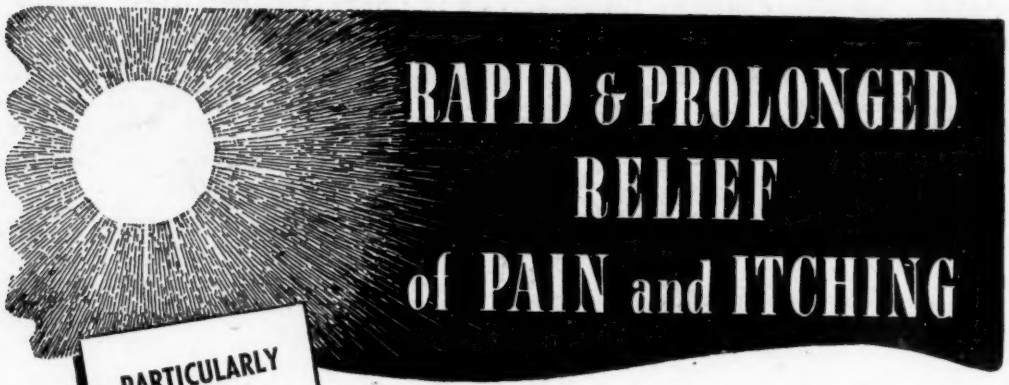

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